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DISEASE PROCESSES VERSUS DISEASE PICTURES IN INTERPRETATION OF RETINAL VASCULAR LESIONS

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I AM deeply grateful to the officers and members of the Chicago Ophthalmological Society for the honor of this lectureship and for the opportunity to pay tribute to Dr. Gifford's memory. I trust that I may be forgiven if I take a moment of the time of this scientific society to say a few personal words, for I loved Sandy very much. He was to me not merely an eminent and distinguished colleague but also a great person. I had somehow expected that he and I would grow old in ophthalmology together. Hardly a month passes but that some problem arises on which I wish I could have his judgment, some action in which I know I could have counted on his support. The subject which I have chosen is one in which he was deeply interested.[1]

The past ten years has witnessed a phenomenal increase in knowledge of the pathogenesis of hypertension without a corresponding advance in the field of ophthalmoscopic interpretation. Moreover, many ophthalmologists have been compelled to devote most of their energies to war work during the past years, and the return to their more permanent interests affords an opportunity and a need for reorientation. The time seems opportune, therefore, for a general reconsideration of ideas about retinal vascular disease. What I present here contains little new information, and, indeed, no new conclusions. The old unsolved questions still remain, but if, in the light of present knowledge, they can be formulated more specifically than before, one small step toward their solution will be made.

For three generations ophthalmologists have struggled with the problem of retinal vascular disease chiefly in terms of the definition

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From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

1. Gifford, S. R., and Marquardt, G.: Central Angiospastic Retinopathy, Arch. Ophth. **21**:211 (Feb.) 1939. Gifford, S. R.: Ocular Complications of Diabetes, M. Clin. North America **12**:423, 1928. Gifford, S. R., and MacPherson, W. A.: Classification of Vascular Fundus Diseases, Quart. Bull., Northwestern Univ. M. School **14**:65, 1940. Gifford, S. R.: Proliferating Retinopathy in Diabetes, ibid. **17**:252, 1943; Evaluation of Ocular Angiospasm, Tr. Am. Acad. Ophth. **48**:19, 1943; Eye in General Diagnosis, Wisconsin M. J. **43**:509, 1944; Evaluation of Ocular Angiospasm, Arch. Ophth. **31**:453 (June) 1944.

and description of ophthalmoscopic pictures. They have asked themselves, What is the typical ophthalmoscopic picture of a given class of cardiovascular disease, or, alternatively, what is the typical general clinical syndrome that is associated with certain ophthalmoscopic picture? So long as the internist's and the general pathologist's knowledge of cardiovascular-renal disease was vague and diffuse, the effort to define and describe ophthalmoscopic pictures was useful and appropriate. The classifications established by the ophthalmologist were not more vague or ill defined than those of the internist. There were, indeed, some cases of "albuminuric retinitis" in which there was no albuminuria, some cases of diabetic retinitis in which the diabetes was mild and inconspicuous, some cases of senile changes in the fundus which had to be called "juvenile"; but these exceptions were not numerous or disturbing to the *amour propre* of the profession, smugly content in the assertion that its members alone of all the medical fraternity could look at the blood vessels in the living patient and render a final verdict.

With the refinement in classification and analysis by the internist, sharper disease groups have been established. Ophthalmologists have attempted to keep pace with these developments and have formulated parallel classifications of ophthalmoscopic pictures. I do not wish to disparage these efforts. I have, in fact, contributed my own share to this work.[2] The statistical analyses of correlations between ophthalmoscopic and general clinical findings furnish solid steps in the slow and laborious advance in knowledge of disease. But it is immediately apparent to any one who attempts to apply one of the modern systems of classification of changes in the fundus that the correlations are merely statistical, that the sharper the classification is made the more individual cases which are improperly classified will be found. It would seem worth while, therefore, to stop for a moment one's search for the typical and the probable and ask oneself what conclusions are to be drawn from the atypical and the concrete. What are the disease processes that underlie both the typical and the atypical occurrences?

VASCULAR DISEASE PROCESSES

Up to the present, four major, potentially independent, processes of vascular disease have been recognized: (1) senescence, (2) atherosclerosis, (3) the hypertensive arteriolosclerotic process and (4) diabetic vascular disease. I am leaving out of this account such rare phenomena as periarteritis nodosa and Mönckeberg's sclerosis. With respect to these four major processes, one must ask: What are the

2. Friedenwald, J. S.: (*a*) Retinal Arteriosclerosis, in Cowdry, E. V.: Arteriosclerosis, New York, The Macmillan Company, 1933; (*b*) Retinal and Choroidal Arteriosclerosis, in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, London, Butterworth & Co., Ltd., 1940.

ophthalmoscopic signs by which they are recognized, and how reliable are those signs? What is known as to the mechanism of their development? To what extent are these mechanisms dependent on or influenced by local processes? To what extent are these potentially independent mechanisms also potentially interrelated?

Changes of Senescence.—The concept of the senescent changes in the retinal vascular tree [3] is, in the first place, based on the ophthalmoscopic pictures seen in the fundi of aged persons. In broad outline, the typical ophthalmoscopic picture of senescence includes vessels which are narrow and straight, which branch at acute angles and which show diminished intensity of the vascular light streak. Retinal luster is decreased. There are associated degenerative changes, such as colloid excrescences on the lamina vitrea and atrophic changes in the choroid about the optic disk, in the macular region and in the periphery of the fundus. How reliable are these signs as indications of senescence of the cardiovascular system, or even of senescence in general? It is common experience to see narrow, straight arteries in middle-aged people with atherosclerosis and without other signs of exaggerated general senescence. Furthermore, the high incidence of atheroma of the central retinal artery at the point of its passage through the cribriform disk and within the optic nerve immediately behind the disk has been well established. A detailed correlation of the caliber and tortuosity of the retinal branches with postmortem studies of the structural changes in the artery within and behind the disk is still lacking, but there is at least presumptive evidence that the narrow, straight retinal arteries of the aged are to be attributed to atherosclerosis rather than to senescence.

In this connection, it should be pointed out that Wagener and his colleagues stated that the picture of narrow, straight arteries was characteristic of the first stage of essential hypertension and expressed the belief that it was due to a diffuse spastic contraction of the ophthalmoscopically visible arterial tree. My own experience has led me, on the contrary, to the conclusion that in the early stages of essential hypertension without atherosclerosis the visible portions of the retinal arterial tree are either normal or, in some cases of the severest form, dilated.

The atrophic and degenerative changes occur not only in the aged but also in presenile persons. In fact, their occurrence without senility is so striking that ophthalmologists have been forced to set up separate disease categories for these so-called juvenile cases. Histologically, these atrophic and degenerative conditions are associated with fibrosis

3. Friedenwald, J. S.: The Eye, in Cowdry, E. V.: Problems of Ageing, ed. 2, Baltimore, Williams & Wilkins Company, 1942.

and hyalinization of the choroidal capillaries. The question is still unsettled whether these histologic changes are specific evidence of senescence of the affected tissues, independent of systemic disease; whether they represent a special vascular disease process, distinct from the four major categories previously enumerated, or whether they are the form that the atherosclerotic process takes when it involves vessels of capillary dimensions. The last possibility has certainly not been ruled out and is, in fact, subject to experimental approach, for a quite pure form of atherosclerosis can be produced in rabbits experimentally. In any case, the ophthalmoscopic finding of these so-called senile degenerative conditions is an unreliable index of the state of senescence of the patient's vascular system as a whole.

Finally, there is the senile loss of retinal luster. The explanation of this optical phenomenon involves the solution of a paradox. Biochemical studies have shown that the retina, like other fixed tissues, tends to lose water with advancing age. Its index of refraction should, therefore, increase, and, other things being equal, its luster should also increase. The solution of this paradox must lie in senile changes in the vitreous, rather than in the retina. A possible optical explanation need not be elaborated here, but it is at least apparent that this feature of the senile fundus picture is not concerned with the state of the connective tissue system, including the "vital rubber" of the cardiovascular system. It is, of course, probable that a statistical correlation could be established between the decline in retinal luster and the loss of elasticity in the vascular tree. The passage of the years brings about changes in all tissues, but if the tissue systems are not identically influenced the correlation between vascular elasticity and the calendar age or between vascular elasticity and the facial and bodily appearance may be closer and more reliable than that between vascular elasticity and retinal luster. The fact that retinal luster declines more rapidly in myopic than in hyperopic persons indicates that local factors exert an important influence.

There is, in fact, good evidence that the rate of senescence of different tissue systems is more or less independent. Patients with senile dementia do not, as a rule, show corresponding signs of unduly rapid senescence of organs other than the brain. Their fundi in general have an appearance that correlates much more closely with their calendar age than with their state of mental decline. Conversely, patients with advanced senile changes in the fundus do not in general show a corresponding mental deterioration. There are some organs, like the notochord and the hyaloid vascular tree, which undergo senescence in embryonic life; others, like the gonads, which have a life span considerably shorter than that of the organism, as a whole, and still others,

like the eye, which have a longer potential life span than that of the organism.

In summary, the ophthalmoscopic picture of the senile fundus is made up in part of aspects which can with a high degree of probability be attributed to atherosclerosis; in part of the consequences of capillary fibrosis, which may or may not be an atherosclerotic manifestation, and, in part of senile changes in tissues which are not components of the connective tissue and vascular systems.

This argument obviously begs the question as to whether atherosclerosis and capillary fibrosis are themselves direct or indirect expressions of the process of senescence. A categorical answer cannot be given to this question at the present time, but it seems unlikely that the connection is a direct one. The most general attribute of senile change is the loss of water and of elasticity in the affected tissues,

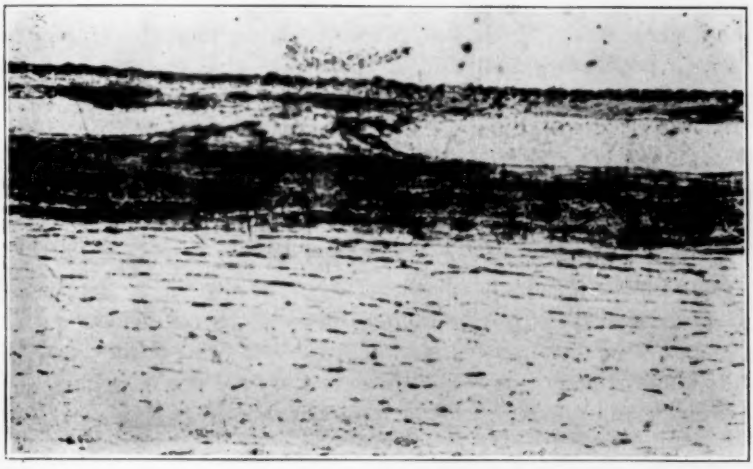

Fig. 1.—Lipid infiltration of the choroid in experimental atherosclerosis in a rabbit.

phenomena which do not appear to be intimately connected with the atherosclerotic process. Experimental atherosclerosis in rabbits is not associated with a general loss of water and of elasticity of the body tissues. On the other hand, histologic study of aging tissues reveals an increase in fibrous trabeculae and of other relatively inert colloidal deposits which encroach on the shrinking microcosm of still vital tissues. Whether these phenomena are related to the atherosclerotic process remains an open question. A number of years ago I had the opportunity to study the ocular tissues of a series of rabbits in which Dr. W. A. Perlzweig, of Duke University, had produced experimental atherosclerosis. A number of these specimens showed extensive lipid infiltration of the choroid. As is well known, these animals also have

a lipid arcus in the cornea. It was evident that experimental atherosclerosis entails a pathologic process more widespread than the mere formation of localized atheromatous plaques in the major vessels. But the fact that there is still a large field of potential investigation in relation to the extent and pathogenesis of the atherosclerotic process should not lead one to overestimate the reliability of ophthalmosccopic findings in the diagnosis of senescence.

Atherosclerosis.—The distribution of atheromas in the vascular tree is spotty and irregular. In no two cases is the pattern identical, though certain points of predilection are fairly well established. No satisfactory explanation has been offered for these points of predilection. It is commonly stated in the textbooks that the frequent occurrence of atheromas at arterial bifurcations is related to special strains occurring at these points, but no hydrodynamic evidence has been advanced to indicate that special strains would in fact exist at these points. Actually, at the orifice of a branch the lateral pressure must be higher than average at the downstream side of the orifice and lower than average on the upstream side, but atheromas commonly surround such orifices, without regard to the slight local differences in pressure. It is likely, therefore, that any explanation of the peculiarities of atheromatous predilection must be based on local anatomic predispositions rather than on special hydrodynamic strains.

One such point of predilection is at the passage of the central retinal artery through the cribriform disk. The narrowing of the vascular lumen peripheral to such a partially obstructive lesion has already been mentioned. If in relation to the atherosclerotic process the vessel also shrinks longitudinally, the retinal branches will be not only narrow but also straight, and the angle of their bifurcations will be narrowed.

This is the ophthalmoscopic picture commonly seen in elderly arteriosclerotic persons with moderate hypertension, the degree of hypertension being closely correlated with the degree of narrowing. A number of years ago [2a] I suggested a possible explanation of this correlation in terms of a close relation between the degree of atherosclerosis of the central retinal arteries and that of the arteries of the brain. If this is correct, the hypertension in cases of senile arteriosclerosis is compensatory and presumably neural in mechanism. No evidence has since been brought forward on this point, and the question still remains open.

The suggestion made here is in contradiction to that of Wagener,[4] who described senile arteriosclerosis as showing reduction of caliber of the retinal arteries and veins without arteriovenous constriction but stated that "there is no actual narrowing of the lumen, so the apparent

4. Wagener, H.: Observations on Retinal Arteriosclerosis, M. Clin. North America **7**:275, 1923.

reduction in calibre must be owing to decreased transparency of the walls."

The interpretation in cases of this type is further complicated by the fact that in atherosclerotic persons atheromas not infrequently develop in the major renal arteries. When such a lesion is sufficient to mimic a Goldblatt clamp, a humoral and renal phase of the hypertensive disease will be superimposed on the previous atherosclerotic phase. Thus, in these cases the transition from essential to malignant hypertension can be reproduced, and in the final state an arteriolar sclerosis may be superimposed on the preexisting atherosclerotic disease. I believe that this course of events accounts for many of the cases in which, both ophthalmoscopically and at autopsy, a mixture of these two processes is shown. An alternative explanation for this common association is given by many recent authors, who assume that hypertension, by producing more mechanical stress on the arterial tree, leads to early and widespread atherosclerosis. Against this interpretation is the fact that patients with coarctation of the aorta carry high pressures in the arteries of the head and arms for many decades without development of atherosclerotic changes.

While the point of maximal predilection for atheroma in the retinal artery is at or behind the optic disk, small lesions of a similar type are not uncommon in the vessels that can be viewed with the ophthalmoscope. Since, as a rule, the wall of the vessel remains invisible, the ophthalmoscopic evidence produced by such a lesion is a local constriction in caliber. Much restraint is required in the interpretation of this feature of the ophthalmoscopic picture, for similar local constrictions in caliber can also be produced by a localized spasm of the arterial wall and by hyaline arteriolar sclerosis. Even the persistence of such a localized constriction for days or weeks does not exclude the possibility of spasm, for previously persistent constrictions disappear promptly in some cases after splanchnic sympathectomy. On the other hand, the spontaneous disappearance of a localized constriction does not exclude the possibility that it was atheromatous, for an atheroma may become partially organized and absorbed. It is only when an opaque spot in the vessel wall is seen associated with a local constriction in caliber that one can assert with considerable confidence that the lesion is atherosclerotic, not spastic. Careful examination of these regions with red-free or monochromatic green light not infrequently reveals a slight opacity, which is less readily visible with white light. When this type of retinal vascular lesion is widely developed, white streaks of appreciable length may be seen on one or both sides of the blood column. In such a case the differential diagnosis between atheroma and hyaline degeneration may at times be difficult. The more diffuse and homogeneous the lesion, the more closely the picture characteristic of hyaline arteriolar sclerosis

is approached. The fact that the two types of lesions may be present simultaneously adds to the diagnostic difficulties.

When the atherosclerotic change affects a retinal artery at the point where it crosses a vein, endothelial proliferation may occur within the vein, and narrowing of the venous lumen may be visible not only at the point of crossing but extending upstream and downstream from that point. The relation of these endothelial proliferations to venous occlusion has been demonstrated by several authors.[5]

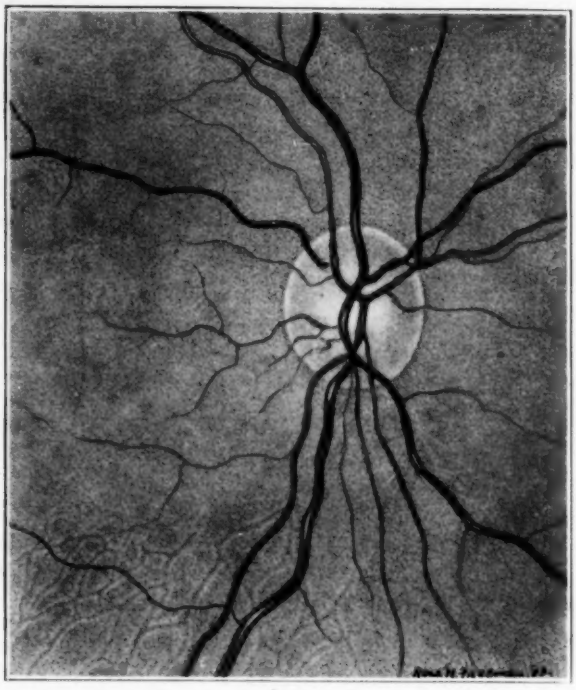

Fig. 2.—The fundus in a case of atherosclerosis with hypertension. The retinal arteries are narrow and straight and branch at relatively acute angles. There are localized caliber constrictions in many of the vessels (possibly due to local atheromas, but this is not certain, since increased visibility of the vessel walls was not observed).

The patient, a white man aged 77, had a blood pressure of 190 systolic and 130 diastolic. There were cardiac enlargement and auricular fibrillation but good compensation. He entered the hospital because of trigeminal neuralgia, for which operation was successfully performed. The urine showed an occasional trace of albumin and some hyaline and granular casts but could be concentrated to a specific gravity of 1.027. The patient showed obvious peripheral signs of atherosclerosis.

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5. Verhoeff, F. H.: Obstruction of the Central Retinal Vein, Arch. Ophth. **36**:1, 1907. Koyanagi, Y.: The Significance of Crossing of Vessels in the Production of Thrombosis of Branches of the Central Retinal Vein, Klin. Monatsbl. f. Augenh. **81**:219, 1928.

Many cases of atherosclerosis are uncomplicated by hypertension. In such cases scattered lesions of the type just described may be seen in the fundi without the general narrowing of the retinal arterial tree. It must be borne in mind, however, that the distribution of atheromatous lesions in individual cases follows a most irregular and unpredictable pattern. Usually retinal atherosclerosis is associated with equally widespread general atherosclerosis, but in the occasional patient the presence or absence of retinal atheromas may lead to a false prognosis. The best preserved man of 87 that I know had at the age of 65 a localized atheromatous plaque in one of his retinal arteries and occlusion of a retinal venous branch. In the following twenty-two years he had had no other signs or symptoms of atherosclerosis, either local or general. Thus, even the more dramatic local vascular accidents furnish relatively

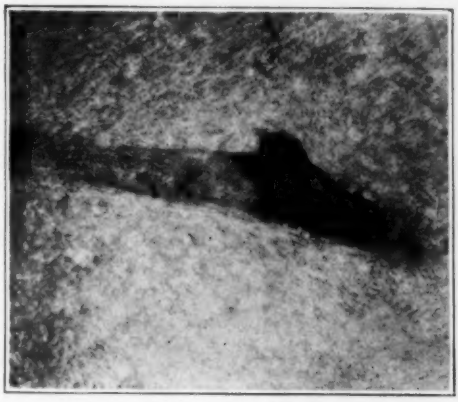

Fig. 3.—Flat preparation of the retina stained for fat, showing an atheroma in an arteriole. The diameter of the arteriole is approximately 60 microns. Magnification, × 100.

uncertain prognostic guides. The important question is not how severe is the local lesion, but how widespread is the process. A small number of atherosclerotic persons exhibit crops of petechial hemorrhages and hard white exudates, resembling those seen in diabetic persons. This group of patients will be discussed in a later section.

Little study has been directed toward the ultimate course of the atheroma itself. It appears to be generally believed that an atheroma once formed remains indefinitely unchanged. This certainly is not necessarily true. Infants under 2 years of age commonly show atheromas in the aorta at autopsy. Infants who survive into childhood almost surely must have had similar lesions which disappeared completely. In experimental atherosclerosis practically complete recovery has also been noted. In the retinal arteries I have seen localized constrictions in

caliber with opacification of the wall of the vessel persist over a year and then disappear completely. The complete resolution of atheromas cannot, of course, be confirmed histologically, but an alternative method of healing can be well demonstrated. One frequently finds atheromas in which

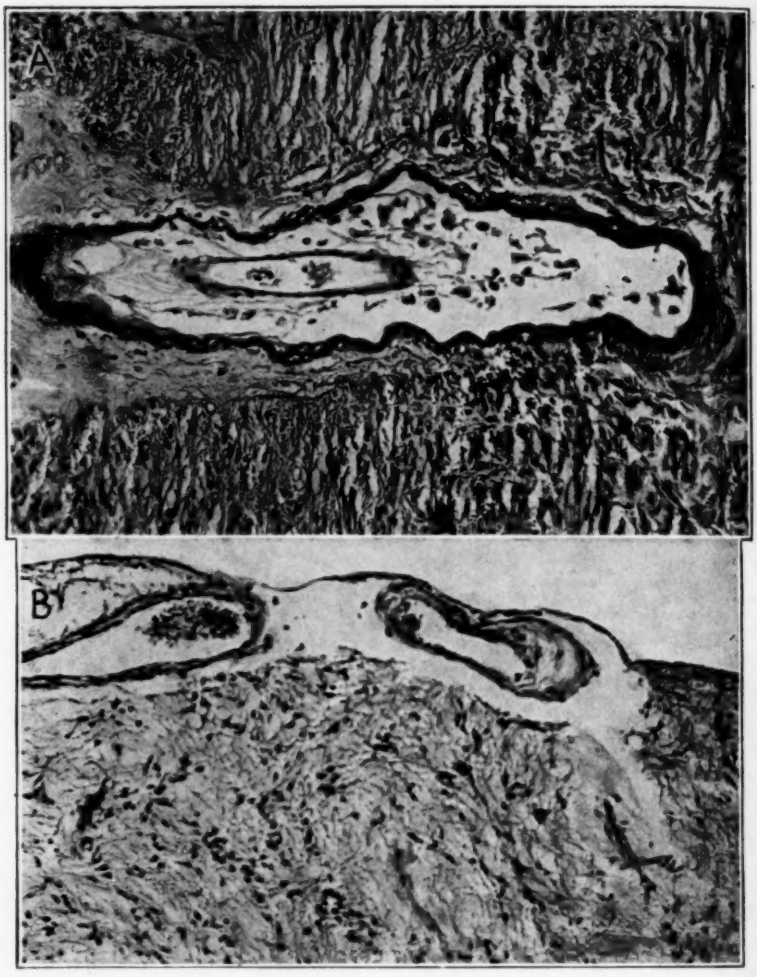

Fig. 4.—*A*, atheroma of the central retinal artery with beginning fibrosis; *B*, atheroma of the major retinal artery with subendothelial fibrosis.

the foam cells are being replaced by a subendothelial scar, which in its crescentic form shows the flattened pattern of the original hillock.

Atherosclerosis of the choroid is a much neglected subject. It has been known for years that the choroid resembles the spleen in the frequency with which its arteries show hyaline degeneration of the

media. Changes of this type are regularly seen in the choroid beginning in the fourth or fifth decade, even in the absence of generalized arteriolar hyalinization. While this is the dominant form of choroidal

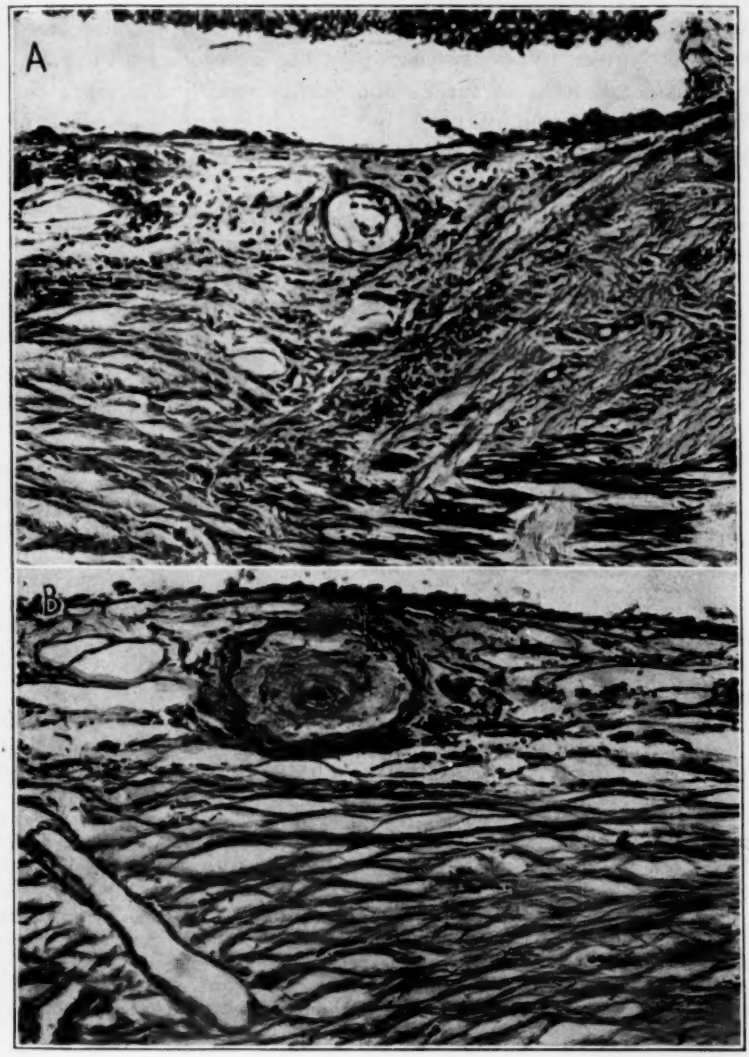

Fig. 5.—*A*, atheroma of a choroidal artery; *B*, atheroma of a choroidal artery with advanced fibrosis.

vascular change, atheromas can also occur. The clinical ophthalmoscopic signs of choroidal atherosclerosis have not even been looked for.

In summary, ignorance of the ocular manifestations of the atherosclerotic process still largely outweighs proved knowledge. In those

cases in which lesions are exhibited in the ophthalmoscopically visible portion of the vascular tree the diagnosis can be made with a relatively high degree of certainty. The signs of sclerosis of the central vessel behind the cribiform disk are still disputed. This was, perhaps, an academic issue when the present differences of interpretation were first formulated, fifteen to twenty years ago, but it becomes an urgent practical consideration in so far as ophthalmoscopic findings are used as guide in the selection of cases for sympathectomy. The relation of atherosclerosis to subendothelial fibrosis and to capillary fibrosis and hyalinization remains unclear.

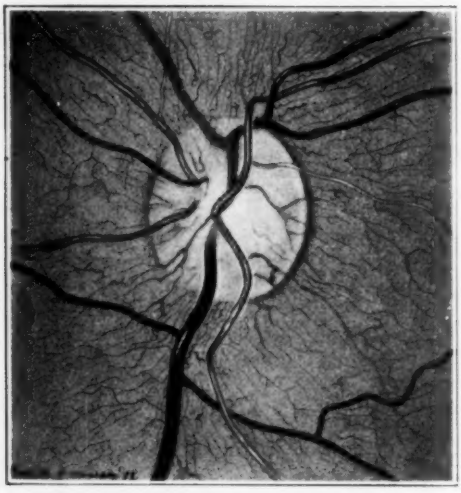

Fig. 6.—Hypertension with beginning arteriolar sclerosis. The general caliber of the arteries in this case was normal, but there were some local constrictions on the inferior branch which appeared and disappeared during the examination (spasm). The arterial walls were visibly thickened at some places, and the arterial light streak showed increased brightness. Arteriovenous compression was observed at only a few vascular crossings (outside the area represented in the drawing).

The patient, a white woman aged 31, had hypertension of nine years' duration and a blood pressure of 240 systolic and 140 diastolic at the time of examination. She had had bouts of hematuria at intervals for seven years, toxemia of pregnancy and a therapeutic abortion eight months before the examination. The urine gave a 1 plus reaction for albumin, but responses to the phenolsulfonphthalein and concentration tests were normal. She died in uremia four years after this drawing was made.

Some of these questions are approachable through the study of experimental atherosclerosis. It is much to be regretted that interest in this field of research, after an enthusiastic beginning, has lapsed. But there are many questions for which no experimental short cut exists and which can be solved only by the slow and painstaking extension of ophthalmoscopic, general clinical and pathologic correlations.

The Hypertensive Arteriolosclerotic Process.—This is the field in which the greatest advances have been achieved during the past decade. Goldblatt and associates [6] demonstrated that renal ischemia in dogs results in severe hypertension, generalized arteriolar sclerosis and progressive renal failure. A number of independent investigators have shown that the disease depends on a humoral factor liberated by the ischemic kidney. The complex nature of the humoral mechanism need not be discussed here. What is of importance is the fact that the malignant phase of hypertensive disease, as defined by Volhard, bears the closest possible resemblance to the experimental disease produced by Goldblatt.

The malignant phase is, in all but the most exceptional cases, preceded by a phase of "benign" hypertension, which may last for many years. The clinical transition from the benign to the malignant phase is generally rather abrupt. Histologic and ophthalmoscopic studies in the later portions of the "benign" phase reveal that hyaline degeneration of the arteriolar walls has already appeared, and the transition from the "benign" to the malignant phase seems to be more a quantitative than a qualitative one, though in the severest forms arteriolar necrosis is added to the previous arteriolar hyaline degeneration.

It has already been pointed out that in patients with atherosclerosis and hypertension renal involvement and arteriolar hyaline degeneration can also develop and the disease thus enter a malignant phase in many respects similar to that which complicates essential hypertension. These two disease processes consequently present many external similarities. To what extent can they be differentiated from one another? To what extent can ophthalmoscopy contribute to the differential diagnosis?

The answers to these questions are by no means simple, and the differential diagnosis in many cases remains unsharp. Age distribution assists in distinguishing many cases. Most patients with atherosclerotic hypertension are over 60, and few are under 50. Most of the patients with nonatherosclerotic essential hypertension have the onset of their hypertension under the age of 50 and have well developed signs of arteriolar hyaline changes in the retinal vessels before they reach 60. Thus, patients under 40 or over 60 years of age present no serious difficulties in the differential diagnosis of these forms. But the age group of 40 to 60 forms an important fraction of the patients for whom the differential diagnosis needs to be made.

6. Goldblatt, H.; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: Studies on Experimental Hypertension: I. Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**:347, 1934. Goldblatt, H.: Studies on Experimental Hypertension: V. Pathogenesis of Experimental Hypertension Due to Renal Ischemia, Ann. Int. Med. **11**:69, 1937.

It is often said that in patients with atherosclerotic hypertension the diastolic blood pressure shows little, if any, rise and that this feature differentiates atherosclerotic from essential hypertension. This asser-

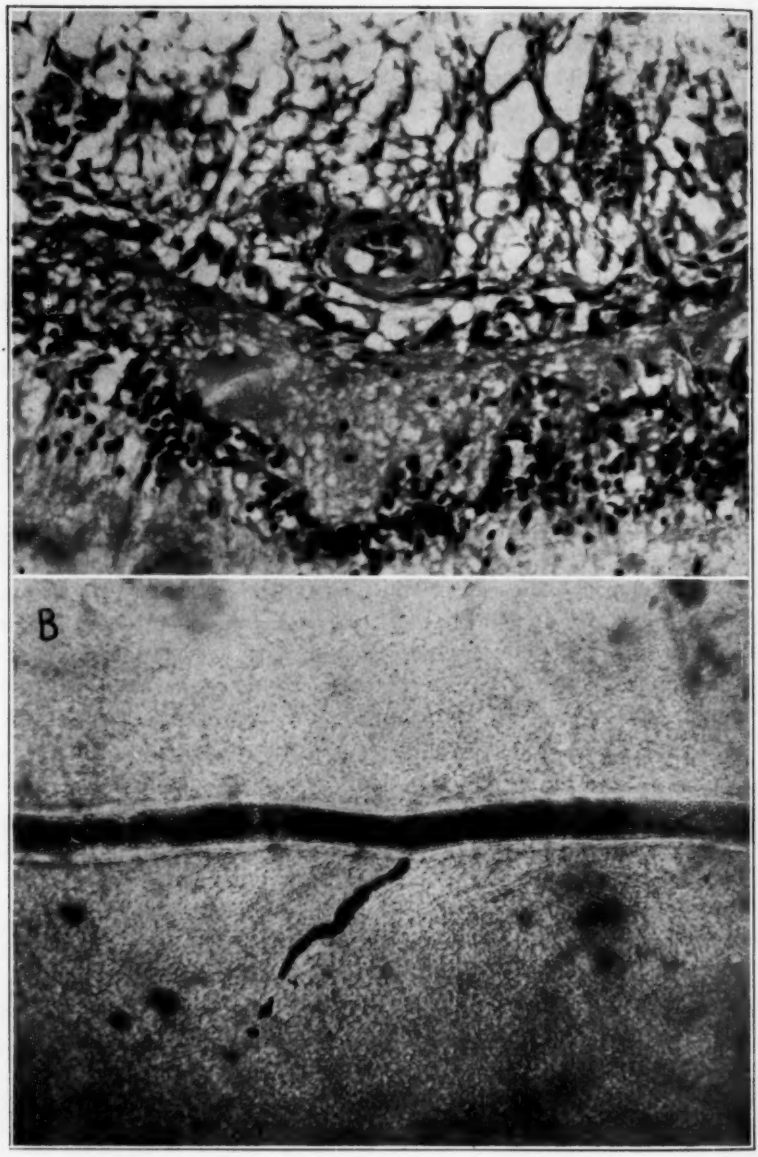

Fig. 7.—*A*, hyaline arteriolar sclerosis; *B*, flat preparation stained for fat, showing hyaline arteriolar sclerosis. Note that the large vessel, which is of the same order of magnitude as that shown in figure 3, has a diffusely thickened, highly refractile wall, while the smaller branch shows, in addition, lipid infiltration.

tion, however, confuses the atherosclerotic process with the senile loss of arterial elasticity, with which it is often associated. Elderly people with normal diastolic pressures but large pulse pressures are not really hypertensive, and they do not contribute to the problem of differential diagnosis which I am now discussing. The group whose condition I have designated as atherosclerotic hypertension consists mainly of elderly people with fixed hypertension. When the disease is well established in these persons, the pressures range from 180 to 220 systolic and from 100 to 120 diastolic.

If one is to use the ophthalmoscope in assisting in the differential diagnosis of hypertension in middle-aged persons, one must first analyze the findings in those age groups in which the differential diagnosis is unconfused. In patients over 60 with moderate fixed hypertension, the retinal vessels are almost always narrow and straight and branch at acute angles. The relation between the degree of arterial narrowing and the degree of hypertension is close. With systolic pressures in the neighborhood of 160, the narrowing is usually just barely perceptible. When the systolic pressure has reached 200, the arteries are reduced to about one-half the diameter of the veins. The correlation between blood pressure and arterial caliber in this group of patients is so close that one can usually guess the pressure rather accurately from the ophthalmoscopic examination. The correlation is, in fact, so close that if an elderly patient does not have as high a blood pressure as the degree of narrowing of the retinal vessels suggests serious consideration should be given to the possibility that an intercurrent disease has lowered the blood pressure below its compensated level.

In patients under 40 with essential hypertension, the retinal arteries are generally of normal caliber and tortuosity. If constriction occurs at all, it is usually segmental or involves only isolated branches, rather than the whole arterial tree. Even when, in the exceptional case, generalized diffuse constriction is present, the degree of constriction is almost always less than that seen in elderly patients with the same amount of hypertension. This description refers specifically to the early stages of the hypertensive disease before extensive hyaline thickening of the retinal arterial walls has taken place. When the hyalinization is well developed, the arterial blood column is often narrow, though the vessel commonly remains tortuous.

With these distinctions in mind, what light can be thrown on the differential diagnosis of hypertension in the middle-aged patient? If the retinal arteries show obvious evidence of hyaline thickening, on the one hand, or of atheromatous plaques, on the other, no serious diagnostic difficulty remains, but if one must be guided merely by observations on caliber and tortuosity, one can do no more than guess. In these circumstances, if the retinal arteries are of normal caliber and

tortuosity, the diagnosis of essential hypertension seems most likely. The same conclusion is to be drawn if the blood pressure is much higher than the degree of arterial narrowing would suggest. On the other hand, if the degree of narrowing of the retinal arteries is proportionate to the hypertension in the sense previously outlined, the case probably belongs to the atherosclerotic group.

Whatever the final decision in this difficult diagnostic problem, the fact remains that in young hypertensive patients there is much less correlation than in elderly hypertensive patients between the degree of the hypertension and the degree of constriction of the retinal arteries. The occurrence of hypertension without constriction of the retinal arteries raises interesting hemodynamic problems. So far as the retinal arterial tree may be taken as a guide, the vascular obstruction in cases of this type would appear to be farther downstream—close to the capillaries—than in cases in which the ophthalmoscopically visible branches are narrow.

As the essential hypertension progresses from the "benign" toward the malignant stage of the disease, the hyaline arteriosclerotic process can be observed in its purest form. There is an increased thickness of the arterial wall fairly diffusely distributed over the whole retinal arterial tree, but often more pronounced in some portions than in others. The thickening of the vessel walls can often first be suspected when there is an increased brightness and width of the arterial light streak, giving the vessel a coppery appearance. This particular ophthalmoscopic sign is one about which many observers find it difficult to be objective. Moreover, the width and brightness of the vascular light streak are greatly influenced by the size of the pupil and by the illuminating system of the ophthalmoscope. A more reliable sign of thickening of the arterial wall is the separation of the arterial and the venous blood columns at the points of their crossing. This manifests itself in an indentation of the vein when it lies under the artery and a knuckling forward of the vein when it lies over the artery.

With the best resolving power in the ophthalmoscope, the hyalinized vessel walls often become visible as a glassy coat surrounding the blood colunm. Those who have used the slit lamp hand ophthalmoscope will be familiar with the fact that by focusing the image of the illuminated slit close to, but not on, a retinal vessel, and thus illuminating the vessel with light reflected from the choroid, the surface of the vessel wall becomes visible as a glassy cylinder. By comparing the diameter of the vessel wall made visible in this way with the diameter of the blood column on direct illumination, a fairly reliable estimate of the thickness of the vessel wall can be reached. The unevenness of the process of hyalinization often leads to localized variations in the width of the blood

column. Often these localized narrowings are associated with rather sharp right angle bends in the vessel.

As the malignant phase of the disease is approached, hemorrhages and cotton wool spots appear. The hemorrhages are most often flame shaped but may be petechial. The cotton wool spots are often spoken of as exudates, but this is a misnomer. The great majority of these fluffy, opaque lesions are focal necroses in the superficial layers of the retina, and on section are seen to be composed of swollen dead cells, presumably glial cells, lying between the bundles of nerve fibers. These are the "cytoid bodies," about which there is an extensive histologic literature. The hemorrhages and cotton wool spots commonly appear in crops. Often their appearance is associated with a sudden exacerbation of the blood pressure. The individual hemorrhages and cotton wool spots usually disappear in a few days or weeks, and if fresh lesions do not develop pronounced improvement in the ophthalmoscopic appearance may take place. Such apparent spontaneous remissions of the disease are common, and great care must be exercised in using the short range course of the ophthalmoscopic picture as an index to interpretation of the effect of a therapeutic procedure.

At a still later stage, neuroretinal edema, with a star-shaped figure in the macula, flat detachment of the retina, and other changes appear. The edema is commonly regarded as the sign of transition from the "benign" to the malignant stage of the disease. However, spontaneous remissions can still occur, even after the appearance of neuroretinal edema. Moreover, as Goldring and Chasis [7] pointed out, an appreciable minority of patients go into the malignant stage and die in uremia without ever having had neuroretinal edema. In order to test the correlation between retinal and renal hyaline arteriolar sclerosis, I studied the kidneys of 20 patients with neuroretinal edema who showed the most extensive hyaline changes in the retinal arterioles. Every kidney showed some glomerular afferent arterioles that were hyalinized, but the extent of the lesion varied from very mild to very severe. Similarly in a series of 20 patients showing the severest hyaline arteriolar sclerosis in the kidney every retina showed some similarly affected vessels, but the extent of the lesion varied from very mild to very severe. Moreover, the hyalinization of the arterioles takes some time, and one occasionally observes in cases of the most fulminating type neuroretinal edema, focal necroses, hemorrhages and exudates without appreciable hyaline changes in the retinal arterioles. This is almost regularly the picture case in cases of fatal eclampsia. It may, however, be argued that eclampsia and malignant hypertension are not identical.

7. Goldring, W., and Chasis, H.: Hypertension and Hypertensive Disease, New York, The Commonwealth Fund, 1944, p. 28.

In many cases of the severe form of the disease, arteriolar necrosis occurs in the retina as well as in the kidney and other organs. Then the endothelium, as well as the media, becomes converted into a structureless hyaline mass, and a fibrinous clot fills the lumen. On ophthalmoscopic examination such vessels appear as white, bloodless cords. However, not every such "silver wire" vessel is necrotic and occluded, for sometimes the hyalinized wall becomes opaque and hides the blood column in one region, though the vessel may still be patent and the blood column still visible in the more terminal portions.

In cases of the atherosclerotic type the approach to the malignant stage of the hypertensive disease is accompanied with a similar development of hyaline sclerosis in the retinal arterioles, complicated, in these cases, by the preceding, and progressive, atheromatous lesions. In these cases the retinal arterial tree generally remains narrow and straight even when the hyaline process has come to predominate in the picture. Often localized atheromatous plaques are seen. Major vascular accidents—arterial and venous occlusions—occur as they do in cases of atherosclerosis in the absence of hyaline arteriolar sclerosis. Sometimes the same branch shows simultaneously the two types of lesions.

In general, the rate of downward progress in the atherosclerotic group is slower, and the duration of the phase of "benign" hypertension longer, than in the nonatherosclerotic group, but this is not invariably the case. Moreover, in many cases of the atheromatous type the malignant stage of the hypertensive disease never develops, but the patient dies instead of a cerebral or cardiac vascular accident or other intercurrent disease. However, the transition to the malignant phase, and the consequent association of atheroma with hyaline arteriolar sclerosis are sufficiently frequent to lead over and over again to confusion about their interpretation. The ancient error is still repeated that atheroma and hyaline degeneration represent the same disease process, differing only in the size of the vessel affected. The fact that these two lesions can be produced experimentally, each in quite pure form, by different and unrelated experimental procedures is solid evidence that the two processes are distinct. Conclusive evidence, however, is found in the retinal vessels, for in retinal arterial branches of the same size and anatomic structure, atheromas may develop in one and hyaline degeneration in another, depending on the nature of the systemic condition. Indeed, when both processes are present, the same retinal vessel can exhibit both lesions.

In the section on atherosclerosis, the mechanism was discussed by which the atheromatous process can lead to malignant hypertension and hyaline arteriolar sclerosis. The role of atheromas of the renal arteries in bringing about this complication has been widely considered in the literature and need not be discussed here. The reverse process, whereby

primary hyaline arteriolar sclerosis might lead to atheroma as a complication, requires comment. It is a familiar fact that some young patients with essential hypertension die of coronary occlusion or cerebral apoplexy, instead of malignant hypertension and uremia. Dr. Alfred Cohn, many years ago, showed me serial sections of the occluded regions in coronary arteries in which he had noted, in the media of the affected vessels, occluded hyalinized arterioles of the vasa vasorum. These observations suggest a possible mechanism whereby, in cases of hyaline arteriolar sclerosis, atheromatous plaques and occlusions of major arteries may develop as complications.

In summary, the course of the hypertensive arteriolosclerotic disease complex can be followed reasonably closely with the ophthalmoscope, though the correlation is not an absolute one. Spontaneous remissions occur in relation to retinal hemorrhages, cotton wool spots and neuroretinal edema, and this must constantly be kept in mind in evaluating supposed therapeutic benefits. Patients in the "benign" phase of hypertensive disease can be divided into two distinguishable groups, which differ from one another not only in their ophthalmoscopic pictures but also in their age incidence and clinical course. Arguments have been presented for regarding one of these groups as primarily atherosclerotic and the other as nonatherosclerotic. I have been unable to find in the literature concerning various therapeutic attempts any clear analysis of the therapeutic results in these two groups considered separately. Perhaps this is because the distinction is of no significance in relation to therapeutic results, perhaps because the same distinction has been achieved by consideration of wholly other criteria. It is generally agreed, for instance, that sympathectomy is not to be recommended for patients over 50, the majority of hypertensive patients with narrow, straight retinal arteries being thus automatically ruled out.

Diabetic Vascular Lesions of the Retina.—In the divisions of the subject discussed in the preceding sections, the important recent advances in knowledge have come from outside the domain of ophthalmology. In the division which I have saved for last, the recent contributions have come chiefly from ophthalmologists. The thorough clinical studies of Waite and Beetham [8] and of Hanum [9] revealed that diabetic retinitis is related much more closely to the duration of the diabetic disease than to its severity. Since diabetic patients under modern care live longer than they did before the use of insulin, the frequency of this complication is increasing. The most careful regulation of the blood sugar seems to

8. Waite, J. H., and Beetham, W. P.: Visual Mechanism in Diabetes Mellitus, New England J. Med. **212**:367 and 429, 1935.

9. Hanum, S.: Diabetic Retinitis: Clinical Studies of One Hundred and Ninety-Five Cases of Retinal Changes in Diabetics, Copenhagen, Einar Munksgaard, 1939.

have little effect in preventing the onset of the retinitis, and no effect at all in preventing the progress of the retinitis once it is well established.

When minute retinal petechiae occur in other diseases, they are regularly absorbed in a few days. The petechiae of diabetic retinitis, however, persist for months, as was first shown conclusively by photographic studies. Balantine and Loewenstein [10] have recently demonstrated that the petechiae are often surrounded by an endothelial

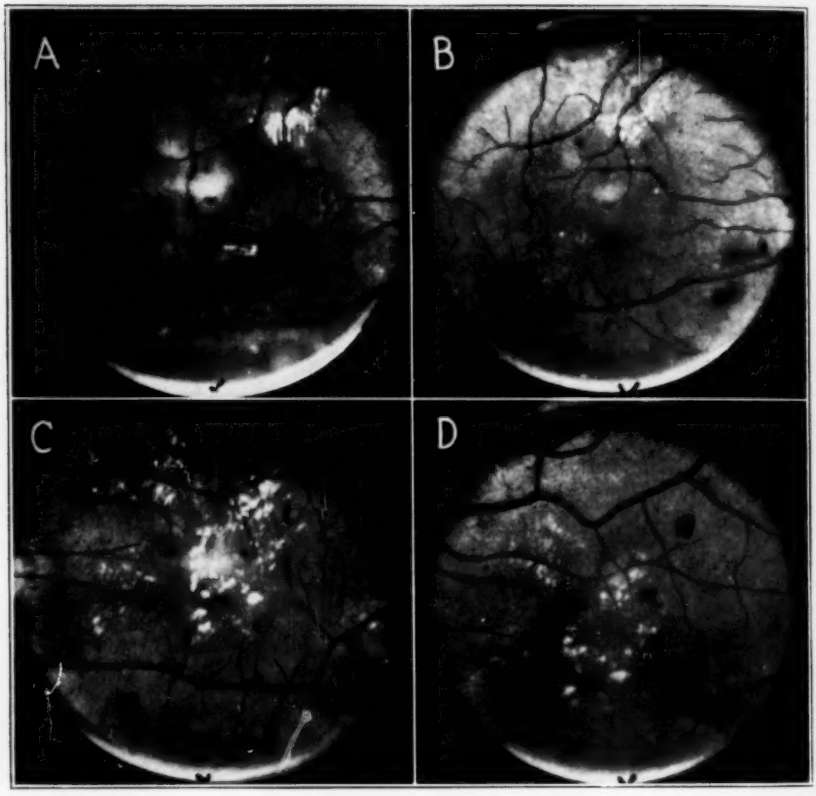

Fig. 8.—*A*, diabetic retinitis; *B*, appearance of the fundus in the same case ten weeks later; *C*, diabetic retinitis in another case; *D*, fundus in the same case ten weeks later.

sac and actually constitute small saccular aneurysms connected with capillaries. I can confirm these observations and, in addition, can report that the aneurysmal sacs are often incompletely lined with endothelium. This indicates that the leakage of blood occurs first, and that the endothelium grows out to cover it afterward. Both the

10. Balantine, A. J., and Loewenstein, A.: Retinal Micro-Aneurysms and Punctate Haemorrhages, Brit. J. Ophth. **28**:593, 1944.

initial persistence of the petechia and its subsequent enclosure by an outgrowth of endothelium suggest that the process develops from a break in the capillary wall, leading to a persistent slow leak of corpuscles. The hole in the wall evidently shows little tendency to heal. Instead, the endothelial cells grow out around the mass of extravasated red cells, eventually forming a minute saccular aneurysm.

If this explanation of the hemorrhages is correct, the accompanying hard white exudates can probably be explained as the consequence of still smaller breaks in the capillary wall through which plasma, but no red cells, escape. The deposit of plasma proteins in the retinal

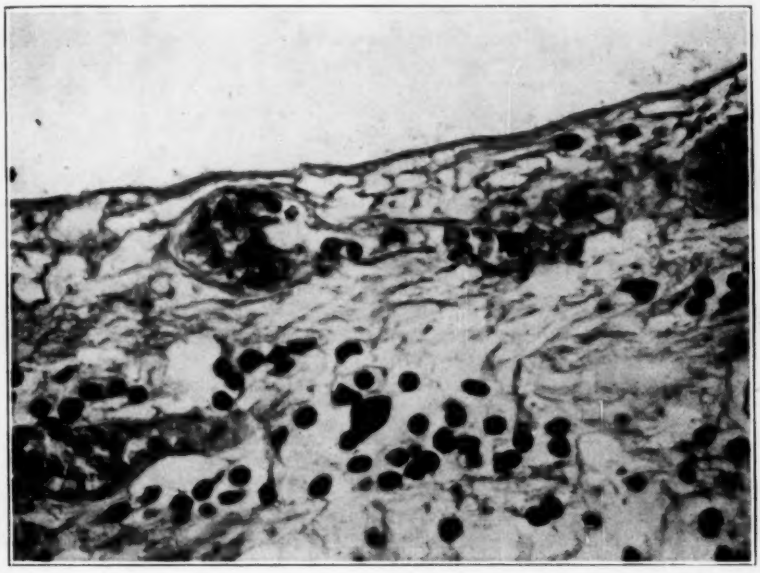

Fig. 9.—Diabetic retinitis, showing a capillary opening into a partially endothelized hemorrhage.

tissue spaces and the inspissation of this deposit as the water filters back into the vascular system would explain the extremely high protein content of these exudates, a feature which distinguishes them from the serous extravasations associated with the neuroretinal edema of malignant hypertension. The photographic studies of Bedell [11] have demonstrated that exudates in diabetic retinitis are not derived from hemorrhages, as was previously thought.

It is difficult to obtain conclusive histologic evidence for the possible course of events here outlined, but indirect evidence is furnished by the

11. Bedell, A.: Fundus Changes in Two Hundred and Five Diabetics, Tr. Ophth. Soc. U. Kingdom (pt. 1) **59**:219, 1939.

report of Hanum [9] that patients with diabetic hemorrhagic retinitis show increased capillary fragility. I can confirm these observations. The simplest, and for these cases the most reliable, test of capillary fragility is performed by placing a blood pressure cuff around the upper part of the arm and inflating it to a pressure of 100 mg. of mercury for three minutes, or to a pressure of 80 mm. of mercury for five minutes.

After the cuff is removed, the arm is held elevated for a few moments to relieve the congestion and to make the petechiae stand out more sharply. Normal persons show no petechiae or at most twenty to thirty. If more than fifty petechiae develop, the test is certainly positive.

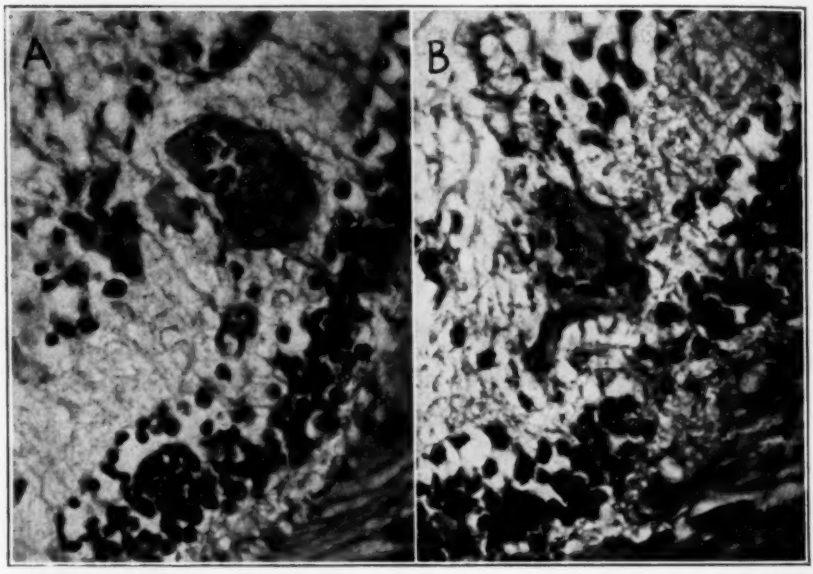

Fig. 10.—Diabetic retinitis. *A*, capillary and adjacent hemorrhage; *B*, adjacent serial section, showing connection between the capillary and the hemorrhage.

Many patients with diabetic retinitis tested in this way show innumerable petechiae not merely in the antecubital fossa but on the wrist and the dorsum of the hand. In my experience, all patients with diabetic retinitis exhibit more petechiae than the average normal subject, though some are within the normal range. The vascular stasis and cyanosis produced by this method of testing for capillary fragility appear to facilitate the development of a positive response in these patients, for the suction test for capillary fragility, which is generally regarded as a more refined method, while confirming the results with the pressure cuff, does not reveal quite so sharp a distinction between patients with diabetic retinitis and the normal controls. The results for diabetic patients without retinitis tested by either method fall within

the normal range. There seems to be no doubt that the retinitis is a manifestation of a general capillary abnormality. How this abnormality is related to the metabolic disturbance of the diabetic patient is still a mystery.

It might be supposed that postmortem studies of the viscera of diabetic patients would throw light on the condition of their capillaries. Unfortunately, I must report that in my hands such a study has been unavailing. I have searched microscopic sections of the viscera of 10 diabetic patients with retinitis, comparing them with the viscera of 10 diabetic patients without retinitis but of approximately the same ages. All 20 patients showed numerous petechial hemorrhages in the viscera, and no difference could be seen between those with retinitis and those without retinitis. Furthermore, patients do not nowadays die of diabetes. Diabetic persons die of infectious diseases, surgical shock, carcinoma or other intercurrent disease, all of which are associated with petechial hemorrhages in the viscera as a terminal event. It is therefore extremely difficult to find autopsy material devoid of such complications. It would seem that one must wait for the experimental production of diabetic retinitis for a deeper attack on its pathogenesis.

The relation of diabetic retinitis to atherosclerosis has long been the subject of discussion. Before insulin was available, all juvenile diabetic patients died after a relatively short illness. Consequently, diabetic retinitis was seen almost exclusively in elderly persons and was usually associated with evidence of generalized atherosclerosis. With modern treatment, cases of juvenile diabetes have appeared in increasing numbers, and in many of these there are no recognizable clinical signs of atherosclerosis. Among the 10 diabetic patients with retinitis in the postmortem study reported in the preceding paragraph was 1 who died at the age of 26 and who had shown no clinical signs of atherosclerosis. The aorta of this patient, however, did show small atheromatous plaques, and none of the other 9 patients were completely free from similar lesions. The importance of this observation, is, however, open to debate, for the question is not whether a sclerotic plaque exists in some remote organ but whether local atherosclerosis in the retina is responsible for the retinitis. The answer to this is unequivocally "no." Many patients are seen clinically without any signs of sclerosis in the ophthalmoscopically visible vessels. I have studied serial sections of the eyes of several such patients without seeing any evidence of atherosclerosis of the retinal vessels. Though the unknown systemic condition which produces atheroma may perhaps be present in all patients with diabetic retinitis, as indeed it is in practically all persons beyond youth, the retinal vessels in many patients show no lesions other than the capillary aneurysms. The only valid question, therefore,

is whether the capillary disturbance in these persons is itself an atherosclerotic manifestation.

The answer to this question is complicated by the fact that some elderly persons with obvious atherosclerosis and without diabetes show petechial retinal hemorrhages and hard white spots of exudate similar to those seen in diabetic patients. H. Friedenwald [12] reported many years ago that approximately one third of the patients presenting this ophthalmoscopic picture failed to show glycosuria. This was before the days of blood sugar measurements and sugar tolerance tests, and it may be that some of the patients without glycosuria had, in fact, mild diabetis. Even with modern methods of testing, however, a small group of nondiabetic patients remain. The nature of the retinal lesions in these nondiabetic patients has not been studied histologically, but there is one clinical feature that serves to distinguish them from true diabetic retinitis. The individual petechial hemorrhages in these patients persist only a few days, instead of months, as in the diabetic patient. It seems likely, therefore, that the pathologic process is different, however closely the ophthalmoscopic picture may resemble that of diabetic retinitis. There is, therefore, little evidence remaining to support the hypothesis that diabetic retinitis is an atherosclerotic manifestation.

The course of diabetic retinitis is in general progressive, but careful studies with repeated photographs of the fundus reveal the fact that there may be many months between the appearance of fresh lesions. Moreover, the individual petechiae and exudates eventually disappear, even though months are required for this to happen. If these patients are examined frequently over long periods in the early stages of the disease, spontaneous remissions can almost always be observed, and this must be borne in mind in evaluating therapeutic results.

COMMENT

The effort to account for differences in ophthalmoscopic interpretation of retinal vascular disease and for discrepancies between ophthalmoscopic and general clinical diagnoses has necessarily been a discursive one. I hope that this has not obscured some conclusions which seem to me quite clear.

1. For the most part, what one sees of the retinal vascular tree is the blood column of the larger vessels. Conclusions as to the functional and histologic processes in the vessel walls based on observations of the blood column are necessarily inferential and subject to error and dispute.

2. The basic processes which affect the vascular tree, which are potentially independent disease entities and which can occasionally be

12. Friedenwald, H.: Retinitis Diabetica, Arch. Ophth. **20**:544, 1891.

observed in pure, uncomplicated form, are also, in varying degrees, potentially interrelated, so that the combined occurrence of several different processes is frequent. The hypotheses which have been presented here as possible explanations of these interrelations and as possible ways of accounting for the frequent existence of impure and complicated cases, are presented as a framework for the ordering of ideas, not as final conclusions. Evidence of varying weight supports them, but they are as yet unproved.

3. In every aspect of the subject there are problems awaiting attack by methods already available. At no time in the last twenty years has the subject of retinal vascular disease presented more enticing opportunities for clinical, pathologic and experimental study.

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AIMS AND AIDS IN THE TEACHING OF BASIC SCIENCES IN OPHTHALMOLOGY

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STUDY of the basic sciences as applied to the eye gives promise of becoming a regular part of the prospective ophthalmologist's training. Some institutions already require such a study before accepting a candidate for a clinical residency; presumably, an increasing number of others will do so in the future. In the belief that experience in organizing and conducting such a course at the Harvard Medical School may be of use to others, the aims of the course as it is now given and certain of the laboratory technics which have been found most practicable [1] are presented in this paper. The writing of it has been prompted by inquiries from those who are proposing to set up basic science courses in ophthalmic institutions elsewhere.

AIMS

A basic science course in ophthalmology should aim primarily to lay a foundation for the appreciation of clinical ophthalmology. It should be to the ophthalmic education at the graduate level what the preclinical subjects in the medical school, usually those of the first two years, are to the general medical education at the undergraduate level. Just as it is important for the medical school student to devote a considerable portion of his time to the study of the basic subjects, it behooves the prospective ophthalmologist to spend whatever time is necessary to learn the application of these subjects to the organ that is to be the basis of his professedly specialized knowledge. Moreover, a course in the basic sciences at the graduate level not only should provide fundamental knowledge about the eye but, what is of equal importance, should also generate a set of standards and a critical judgment by which the student may properly evaluate clinical and laboratory work.

The basic science course bridges the field of general medicine and the specialty of clinical ophthalmology. In no other specialty are there such disciplines required in what may be called the borderlands of

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1. The course has been developed with the assistance of Henry Allen, M. D.; Russell Carpenter, Ph.D.; W. Morton Grant, M.D.; V. Everett Kinsey, Ph.D.; Sumner Liebman, M.D., and Elek J. Ludvigh, Ph.D.

medicine. Physical optics is one example; the complex fields of stereopsis, accommodation and transmissibility of various types of radiant energy are others. Then there are fields which may be touched on in the general medical curriculum but should be elaborated for the prospective ophthalmologist. Examples are the visual purple mechanism in the retina, osmotic forces in the cornea and fluid movement across the blood-aqueous barrier, to mention but a few. These subjects have little significance for the average medical trainee, but for the ophthalmologist they merit special study.

Some eager persons, to be sure, will obtain adequate training without a course. Organized training can offer to these persons only a more efficient means of obtaining the information. But it is not for them that the courses are primarily intended. It is for the average person who is to take a clinical internship and who will otherwise get only a superficial knowledge of the basic sciences.

The success of the course must depend in large measure on the faculty. While a sympathetic administration is desirable and adequate space is practically essential, it is nevertheless the teachers who will make or break the course. Too often in postgraduate teaching, as in other affairs, the organization is set up and the teaching staff is taken for granted. This is because the courses are set up by organizers and not by the teachers themselves. Emphasis should be put on the teachers and the course organized about their qualifications. This is accomplished in practice by allocating time according to what the teacher has to offer. To omit a subject is less of an evil than to have it taught poorly.

The following subjects as applied to the eye and the percentage of time allotted to each are suggested as a tentative schedule, to be varied according to the teaching capabilities available. Pathology is incorporated with the clinicopathologic course which follows the basic course and is therefore not listed in the following schedule.

	Percentage
Anatomy, histology and embryology	23
Physical and physiologic optics	23
Physiology and biochemistry	19
Neuroanatomy and neurophysiology	18
Bacteriology	8
Pharmacology and toxicology	4
Ophthalmic instrumentation	4
Miscellany (heredity, electroencephalography)	1

It is best that the teaching of these specialized subjects be done by persons who are actively working in the field of ophthalmology. Such persons are to be found almost exclusively in ophthalmic research centers. The teaching should not be farmed out indiscriminately to members in the basic science departments in the medical school who have had no special interest in the eye nor to clinicians who have had little

contact with the basic sciences. In so far as there are few ophthalmic centers at present having the personnel trained in the basic sciences, the courses, at present, should be given in only a limited number of places. The classes should be sufficiently large, however, to supply the residents for the many clinical institutions which do not have the basic science facilities.

The course should be taken by a student just prior to his ophthalmic residency if possible, but in any case not during the residency. Since much study and freedom of mind are required, it is inadvisable to mix clinical work with the basic studies, especially when the preoccupying duties of a house officership are involved. The duration of the preclinical course should be a minimum of twelve weeks' full time study; approximately one half of the classroom time should be laboratory exercises.

AIDS

It is the purpose of this section to describe some demonstrations and experiments which have been found especially useful in the students' laboratory sessions. Since much of the laboratory work in ophthalmic basic science courses is new, most of the exercises here described have been developed *de novo*. It would be helpful if other instructors would similarly report their teaching aids as developed.

The laboratory work in anatomy consists of dissection of the human orbit (not more than two men to an orbit) and the gross dissection of beef eyes. In embryology and histology, it consists of microscopic study of slide material prepared from animal and human eyes. The sections from human eyes are prepared as serial cross sections of the globe, stained at regular intervals with different dyes to show the various histologic structures and yet permit reconstruction of the whole eye.

The laboratory work in physiology revolves about the following subjects: corneal permeability and corneal swelling (experiments similar to those previously described) [2]; permeability of the blood-aqueous barrier as determined by transfer of fluorescein into the eye and the effects of various drugs on it; mechanism of aqueous humor formation, as determined by vital staining of the ciliary process [3] and transfer of ascorbic acid into the eye [4]; effect of ultraviolet radiation on the cornea

2. Cogan, D. G., and Kinsey, V. E.: The Cornea: I. Transfer of Water and Sodium Chloride by Osmosis and Diffusion Through the Excised Cornea, Arch. Ophth. **27**:466-476 (March) 1942; The Cornea: III. Hydration Properties of Excised Corneal Pieces, ibid. **28**:272-284 (Aug.) 1942; The Cornea: IV. Hydration Properties of the Whole Cornea, ibid. **28**:449-463 (Sept.) 1942.

3. Friedenwald, J. S., and Stiehler, R. D.: Circulation of the Aqueous: VII. A Mechanism of Secretion of the Intraocular Fluid, Arch. Ophth. **20**:761 (Nov.) 1938.

4. Kinsey, V. E.: To be published.

and of infra-red radiation on the whole eye [5]; measurement of reducing substances in the lens and of vitamin A in the retina; determination of the absorption spectrums of vitamin A and visual purple with the spectrophotometer; measurement of the accommodative power of the eye (Scheiner's experiment) and of the size of the pupil (objective and entoptic methods); production of experimental glaucoma in the rabbit by ligation of the vortex veins, and observations on autokinetic ocular movements and artificially produced nystagmus (rotatory and caloric stimuli).

The laboratory work in physical and physiologic optics consists of standard optical bench procedures, using a somewhat modified bench,[6] dark adaptation studies, critical flicker frequency measurements, horopter determinations and after-image studies.

The laboratory work in neuro-ophthalmology includes the following exercises: construction of a model eye out of a golf ball [7] to illustrate the mechanics of extraocular muscle action; construction of a brain model [8] showing the ocular motor centers in the brain stem and the visual pathways; drawing of cross sections and longitudinal sections of the brain stem through the third, fourth and sixth cranial nerve nuclei; drawings of the base of the brain, and study of the excellent stereoscopic drawings of the brain prepared by Leinfelder and Allen.[9]

In bacteriologic exercises, the students are instructed in the technics of taking and preparing conjunctival smears and scrapings, including standard stain and culture methods. They are given prepared culture plates of organisms commonly encountered in ophthalmology and are required to describe the colony and cytologic characteristics of the various types of bacteria; similarly, they are held for a description of inclusion bodies and fungi assigned to them. Finally, they are given preparations illustrating the actions of several antibiotics and of anti-antibiotics.

The laboratory work in ophthalmic instrumentation is necessarily varied. Slit lamp biomicroscpy begins with exercises on adjustment and measurement of magnification. Then the student examines with the instrument special optical chambers [10] made to simulate the eye, containing various fluids illustrating the appearance of colloids, particulate matter, blood cells and convection currents. The types of illumination

5. Cogan, D. G., and Kinsey, V. E.: Action Spectrum of Keratitis Produced by Ultraviolet Radiation, Arch. Ophth. **35**:670-677 (June) 1946.

6. Ludvigh, E. J.: To be published.

7. Cogan, D. G.: To be published.

8. Liebman, S. D.: A Model of the Visual Pathways, Arch. Ophth. **27**:1122-1125 (June) 1942.

9. Leinfelder, P. J., and Allen, L.: Unpublished data.

10. Grant, W. M.: To be published.

and structures to be visualized are determined first on the enucleated beef eye and then on the living rabbit eye, with the introduction of such experimental variations as vital staining of corneal nerves and the production of epithelial edema. Finally, the characteristics of the normal human eye are determined by having the students examine each other.

Ophthalmoscopy, direct and indirect, is practiced by the students first on models and then on each other, with the introduction of such variables as color and polarizing filters. Dynamometry is practiced, and the students are asked to compare the diastolic pressure of the retinal arteries with that of the brachial artery. After the angle of the anterior chamber in beef, rabbit and human eyes is examined as far as possible with the slit lamp biomicroscope, various gonioscopic technics are tried, first with a small right angle prism [11] and subsequently with standard contact lenses.

Various types of tonometers (Maklakov, Schiøtz and Souter) are used on animal eyes and on the eyes of fellow students with exercises illustrating the advantages and limitations of each. Finally, exercises are prescribed illustrating the routine procedures in perimetry, campimetry, stereocampimetry and angioscotometry.

Laboratory outlines are given the students to guide them in the foregoing exercises and one or more instructors are always in attendance to volunteer suggestions and to answer questions, but every effort is made to have the student derive his own answers and to reach an independent judgment. It is felt that in this way only will he obtain the measure of self confidence and independence of judgment that is as important as the knowledge derived from the specific experiments themselves.

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11. Grant, W. M.: Unpublished data.

PRIMARY LIPID DYSTROPHY OF THE CORNEA

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DYSTROPHIA adiposa corneae was first described by Kamocki [1] in 1893 in a paper entitled, "A Case of Fatty Degeneration of the Cornea with Intermittent Irritative Phenomena." Katz and Delaney,[2] in their careful review of the cases reported up to 1933, found only 8 undoubted instances of primary fatty degeneration of the cornea. These cases were reported by Kamocki [1] (Warsaw), 1893; Tertsch [3] (Vienna), 1911; Bachstez [4] (Vienna), 1921; Kusama [5] (Tokyo), 1921; Verderame [6] (Turin), 1922; Elschnig [7] (Prague), 1923; Denti [8] (Milan), 1926, and Meyer [9] (Freiburg), 1928. Katz and Delaney also recorded a list of 7 cases that they felt did not fulfil the narrow limits of the condition, in that all occurred shortly after an ocular inflammation. These cases were reported by Takayasu [10] (Japan), 1912; Dor [11] (France), 1913; Meesmann [12] (Berlin), 1928; Spanlang [13] (Vienna), 1927, and Gilbert [14] (Hamburg), 1929. A search of the literature since 1933 has revealed only 3 cases reported as instances of primary fatty dystrophy: a case reported by Katz and Delaney [2] (Chicago), 1933, and 2 cases by Wright [15] (India), 1936.

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1. Kamocki, V.: Arch. f. Ophth. **39**:209, 1893.
2. Katz, D., and Delaney, P. A.: Dystrophia Adiposa Corneae, Arch. Ophth. **9**:78 (Jan.) 1933.
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4. Bachstez, E.: Arch. f. Ophth. **105**:997, 1921.
5. Kusama: Klin. Monatsbl. f. Augenh. **66**:111, 1921.
6. Verderame, cited by Clausen, W.: Zentralbl. f. d. ges. Ophth. **10**:56, 1923.
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9. Meyer, H.: Klin. Monatsbl. f. Augenh. **81**:786, 1928.
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12. Meesmann, A.: Die Mikroscopie des lebenden Auges, Berlin, Urban & Schwarzenberg, 1928, p. 66.
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The purpose of this article is to report a case of primary lipid dystrophy under observation at the present time. This dystrophy is associated with hypercholesteremia.

REPORT OF A CASE

History.—G. C., a Negro farmer aged 61, was first seen in the medical clinic of Duke Hospital July 12, 1944, complaining of recurring temporal headaches of two years' duration and failing vision of three years' duration. The family history revealed hyperthyroidism in a sister and cardiovascular disease in the father. The past history disclosed that the patient had been struck on the left brow with an ax at the age of 6, without injury to the eye. Physical examination gave the following pertinent findings; oxycephaly; dirty, carious teeth; bilateral corneal opacities; lipoma of the scalp over the occiput; lipoma of the left axilla, and slight enlargement of the left ventricle. The blood pressure was 210 systolic and 115 diastolic. The patient was judged to have hypertensive cardiovascular disease with arteriosclerosis, lipomas and corneal opacities. He was then referred to the eye clinic for diagnosis and treatment of the ocular condition. In the eye clinic, the patient gave a history of "irritation" of the left eye for the previous four years. This consisted of an attack of injection of the conjunctiva, pain and lacrimation. The inflammation subsided without treatment. This was followed by similar attacks at about three month intervals in the left eye only. "Smoky" vision in the left eye was noted about two years prior to examination. Twelve months before, a similar attack occurred in the right eye, and this was followed shortly by a bilateral attack. At the time of examination the only complaint was diminishing vision in the left eye. The patient had never injured either eye and had had excellent vision until the onset of the present illness.

Examination.—Adnexa were normal. There was moderate conjunctival injection of the right eye. A grayish opacity was present in the posterior layers of the right cornea in a small area just inside the limbus in the lateral aspect. The left eye was white and quiet. Two dense corneal opacities almost completely covered the left cornea from the inner and outer canthi, except for a small area above and below the pupillary area (fig. 1). The opacity was so dense that the iris and pupil could be only vaguely seen and the pupillary reactions could not be determined. It was yellowish white and heavily vascularized from both the inner and the outer canthus. Both eyes stained with fluorescein, and a small spot of superficial ulceration was found at the limbus of the right eye inferiorly. The left eye did not take a stain. Examination of the right eye with the slit lamp revealed no aqueous flare or keratic precipitates. Corneal sensitivity was normal. Vision was 20/20 in the right eye and 20/400 in the left eye. Tension appeared normal to digital examination. The house officer's impression was that of corneal dystrophy of unknown cause, but probably of nutritional origin. Oral administration of vitamins was prescribed, as well as instillation of drops of cod-liver oil for the right eye. Instructions were given to return in three months.

Course and Examination.—On October 24 the patient returned with no complaints. He had had no symptoms since he had been last seen. Vision was unchanged. Examination with the slit lamp showed no change except for increasing density of the opacities in the left eye. Both eyes were white and quiet. No stain was taken by either cornea. No keratic precipitates or flare was seen.

Feb. 13, 1945: The only change noted in the examination was that the opacity in the left eye was much denser and had involved the entire cornea. Vision was 20/20 in the right eye and was limited to light projection in the left eye.

May 15: He returned with the complaint that he felt as though he had had something in his right eye for the past seven days and since then the eye had been painful and injected. He reported no visual change in the right eye. Examination showed that vision in the left eye was limited to light projection. The eye was quiet and white, with a dense corneal opacity. Vision in the right eye was 20/25. There were marked conjunctival injection temporally and a ragged-appearing conjunctival ulcer, 2 mm. in diameter, which stained with fluorescein, just outside the limbus at 9 o'clock. There were multiple, superficial tiny areas of staining over the lower third of the cornea. The deep opacity was unchanged in appearance and size. There was no circumcorneal injection, keratic precipitates or aqueous flare.

May 19: The patient was admitted to the hospital, and the piled-up, ragged tissue was débrided from the ulcer, so that the cauterizing agent would come in

Fig. 1.—Two dense corneal opacities in the left eye.

direct contact with the base of the lesion. It was then cauterized with 7 per cent iodine and covered with a conjunctival flap. The postoperative course was uneventful, and the patient was discharged from the hospital on the fifth postoperative day, at which time the flap was holding well and the area took no stain. Subsequent examinations at two week intervals showed the superficial keratitis to be gradually clearing up, until, on July 12, 1945, the right eye was completely quiet and no area of staining could be found in the cornea.

Aug. 16, 1945: The patient returned, stating that a bug had flown into his right eye a few days ago and since then the eye had become inflamed and painful. Examination, surprisingly, revealed a macerated black bug in the lower conjunctival fornix. It was removed. Examination with the slit lamp showed a number of the tiny superficial areas of staining on the lower third of the cornea. The opacity had definitely progressed toward the pupillary area and had also involved more of the substantia propria near the limbus. A few tiny vessels could be made out entering it in the middle of the substantia propria. No keratic precipitates or aqueous flare was seen. There was moderate conjunctival injection.

For the first time a fatty degeneration of the cornea was considered. Instillations of 1 per cent atropine and an ointment containing vitamins A and D were prescribed, and he was told to apply hot compresses to the eye as often as possible. Admission to the hospital was suggested, but the patient wanted to harvest his tobacco crop before coming into the hospital.

August 23: One week later, the right eye appeared unchanged except for continued progress of the corneal opacity toward the center of the cornea. It was feared that the same process that had involved the left eye was endangering the right. Arrangements were made to admit the patient for biopsy of the corneal lesions, complete work-up of the case and possible corneal transplant in the left eye.

September 24: The patient was admitted to the hospital. The history and physical examination failed to reveal anything that had not been discovered in the clinics. Examination with the slit lamp at this time showed the following condition:

Right Eye: The cornea showed slight mixed injection (fig. 2*A*). The corneal epithelium appeared roughened and stained with fluorescein in numerous tiny places over the lower third of the cornea, forming minute dots and larger, confluent areas. No superficial infiltration was present. The lesion of interest was a smudge of whitish, greasy-appearing material, which extended along the posterior layers of the cornea from the temporal limbus in a crescent-shaped, diffuse opacity from 7:30 to 10:30 o'clock. It began immediately in front of Descemet's membrane and extended forward into the stroma to various depths but never more than through half its thickness. There were tiny, glittering particles in this area which were a dull gold. There was little vascularization, although a few small vessels extended into the stroma from the limbus in the central portion of the stroma. No keratic precipitates or aqueous flare was seen. The iris and the lens appeared normal.

Left Eye: The eye was white and quiet (fig. 2*B*). The cornea showed dystrophy, which may have been an advanced stage of the process which was beginning in the right eye. Almost all the normal cornea was replaced by a yellowish white opacity, leaving only a small ring of comparatively clear cornea adjacent to the limbus. The opacity was dense and seemed to comprise all the layers of the cornea. It appeared as though all the central portion of the cornea had been replaced by a nodular mass, elongated irregularly and impregnated with small flocculent, chalklike deposits at various depths of the stroma. At various places the surface glittered, but no definite crystals could be seen. The vascular supply was extensive. It was derived from two large vessels, one on the temporal and one on the nasal side. These two large vessels were derived, in turn, from the conjunctival network. Many deeper vessels penetrated into the substantia propria at greater depths and anastomosed with these superficial vessels. The precipitated white matter appeared to follow, to some extent, these vascular channels. The periphery was not entirely free from opacity. In it were small, discrete opacities at various depths. The anterior chamber and the iris could not be made out because of the degree of opacity of the cornea. Ophthalmoscopic examination of the right fundus showed some arteriosclerotic changes in the vessels but no hemorrhages or exudate.

Laboratory Findings.—The white cell count was 8,040. The hemoglobin measured 15.4 Gm. per hundred cubic centimeters, or 100 per cent. The urine was normal. The blood chlorides measured 508 mg. per hundred cubic centimeters; the total proteins, 7.7 Gm.; the albumin, 3.3 Gm. and the globulin, 4.4 Gm., per hundred cubic centimeters. The albumin: globulin ratio was 0.75. The serum

cholesterol (see "Comment") was 390 mg. per hundred cubic centimeters (normal, 250 mg. per hundred cubic centimeters) on September 26, 300 mg. per hundred cubic centimeters on October 10 and 250 mg. per hundred cubic centimeters on

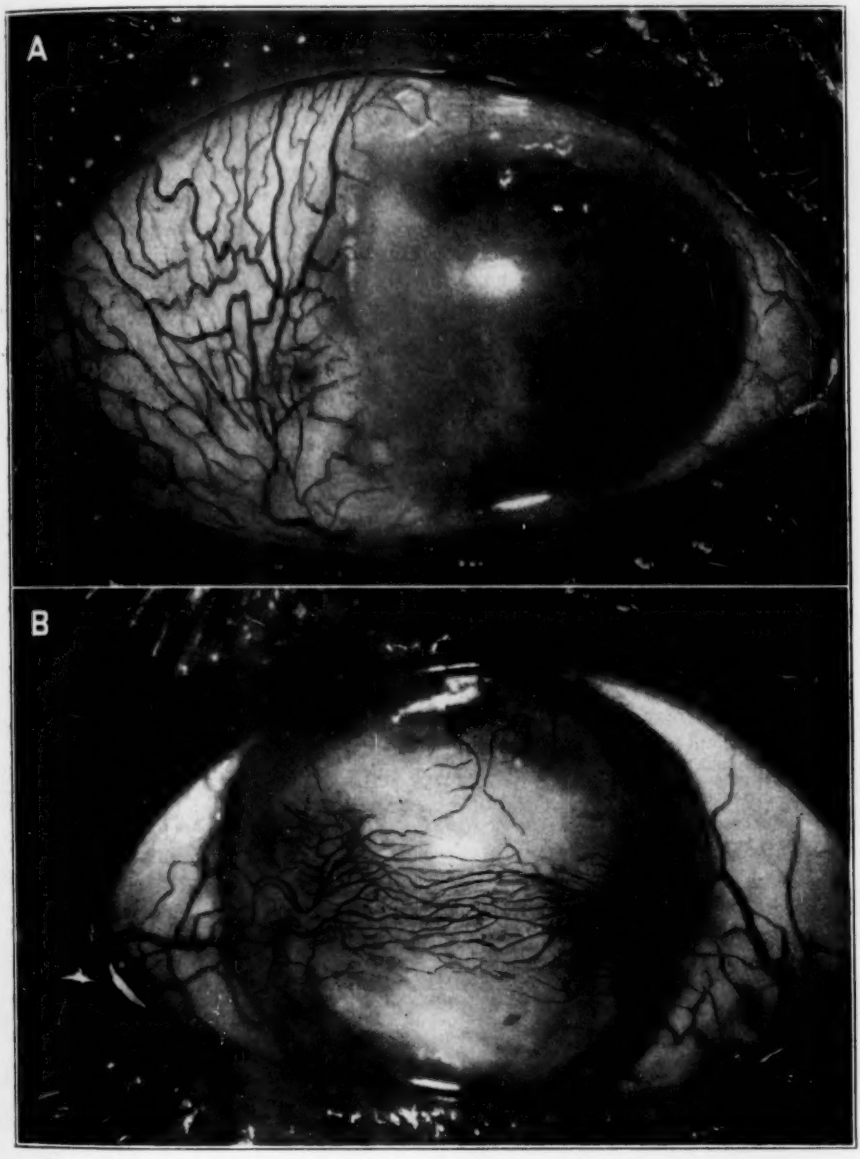

Fig. 2.—Appearance of (*A*) the right eye and (*B*) the left eye.

October 25. The blood sugar measured 105 mg. per hundred cubic centimeters on October 11 and 120 mg. per hundred cubic centimeters on October 13.

The results of the dextrose tolerance test were as follows: The fasting blood sugar was 90 mg. per hundred cubic centimeters; at the end of one-half hour the blood sugar measured 131 mg.; at one hour, 180 mg.; at two hours, 125 mg., and at three hours, 90 mg., per hundred cubic centimeters.

The reaction to tuberculin was positive in a dilution of 1 : 10,000. The Wassermann reactions of the blood and spinal fluid were negative. The basal metabolic rate was —6 per cent.

The skull appeared oxycephalic in the roentgenogram. There was no evidence of Schüller-Christian disease, xanthomatosis or any other condition causing lesions of the skull. A roentgenogram of the chest showed that the lungs were clear. There were moderate widening of the aorta and enlargement of the left ventricle. Roentgenograms of the hands and feet were normal.

A medical consultant could find no evidence of Schüller-Christian disease or of any other xanthomatous condition. He did consider the possibility that the patient had incipient diabetes with a high renal threshold. Neurologic examination and studies of the nose and throat revealed nothing abnormal.

Course in Hospital.—The patient was placed on a high vitamin diet and received 1 drop of penicillin (1 : 2,500) in the right eye every hour and 1 drop of 1 per cent atropine three times a day in the right eye. Compresses of warm boric acid solution were applied to the eye. Two superficial roentgen treatments of 100 r each were given to the right eye one week apart. A scraping from the right cornea made on July 1, 1945 revealed intracellular and extracellular globules of fat, after which a deeper specimen was taken from each cornea for biopsy. On October 13 he was placed on a low fat, low cholesterol diet. A corneal transplant, using a 4 mm. trephine, was made on the left eye on October 16. The iris and lens appeared normal. The patient had an uneventful postoperative course, the sutures being removed on the third postoperative day, and he was out of bed on the tenth day. Five days prior to discharge he was given 20 mg. of thyroid twice daily. Just before discharge the axillary lipoma was removed for examination. Examination with the slit lamp on his discharge, October 31, showed that the right cornea did not take a stain and that the deeper lesion was stable. The transplant was becoming vascularized and looked hazy. Vision was 20/20 in the right eye and was limited to counting fingers at 5 feet (150 cm.) in the left eye. He was told to follow a low fat diet because of the high cholesterol content of the blood.

Pathologic reports on the various specimens submitted were as follows:

A superficial scraping was taken from the involved area of the right cornea, fixed in solution of formaldehyde and stained with sudan IV. Examination showed the presence of a great deal of fatty substance, the bulk of which was extracellular. However, there were many macrophages which contained fatty granules in their cytoplasm. A similar preparation made from a normal cornea failed to reveal any fatty substance. The epithelial cells could not be examined carefully with this stain for fat.

A similar biopsy specimen taken from the left eye and fixed in both Zenker's fluid and dilute solution of formaldehyde U. S. P. failed to stain with hematoxylin and eosin satisfactorily. This problem was also encountered by Berliner [16] in the staining of a cornea removed at autopsy in a case of Hurler's syndrome (lipochondrodystrophy), in which there was a lipid degeneration of the cornea following

16. Berliner, M. L.: Lipin Keratitis of Hurler's Syndrome: Clinical and Pathological Report, Arch. Ophth. **22**:97 (July) 1939.

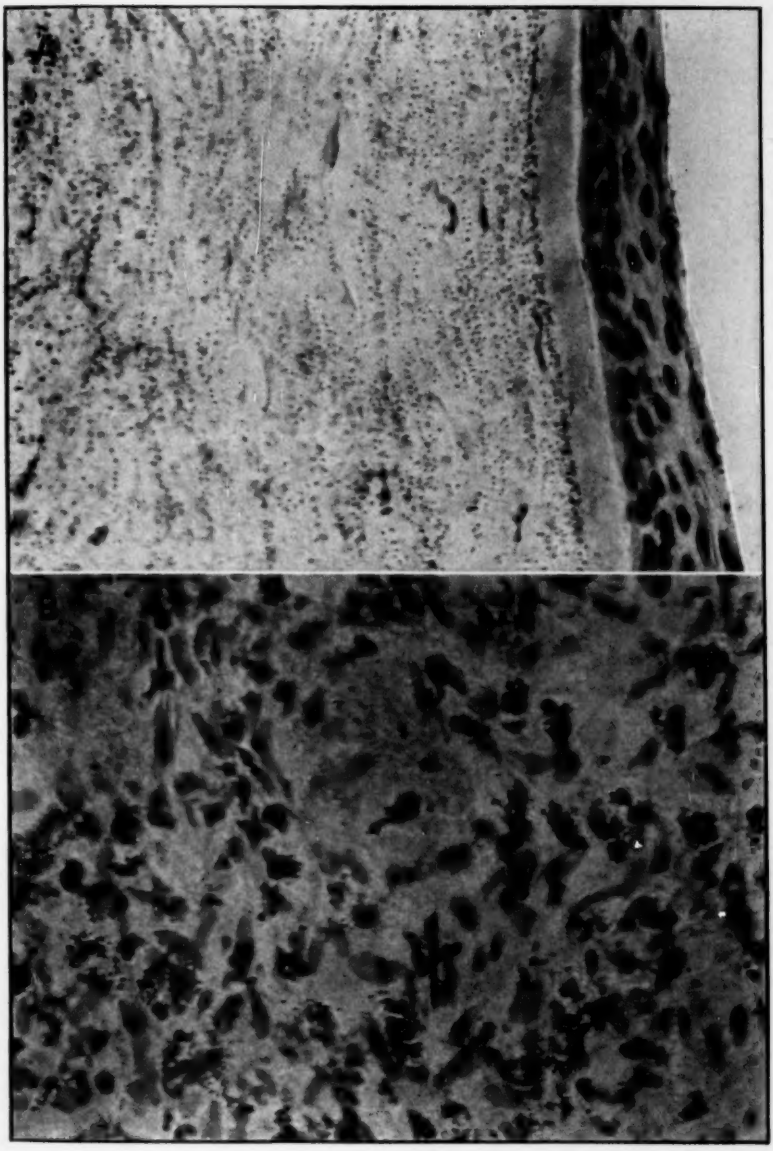

Fig. 3.—*A*, section through disk of cornea removed for corneal graft (hematoxylyn and eosin stain). *B*, section through corneal stroma stained with sudan IV showing numerous intracellular and extracellular fatty deposits.

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keratitis. The tissue took a stain for fat (sudan IV) well, and no fat globules were seen; however, many needle-like crystals, 5 to 10 microns in length, took the stain for fat. Polariscopic examination showed them to be doubly refractile cholesterol crystals. These crystals lay either in the cytoplasm or between the epithelial cells. Bowman's membrane could not be demonstrated in these sections.

The disk of cornea removed in the transplantation operation was sectioned, and one-half was fixed in Zenker's fluid and the other in dilute solution of formaldehyde U. S. P. Again, there was difficulty in securing a satisfactory stain with hematoxylin and eosin. However, after several attempts, one was made in which the cellular detail could be clearly made out (fig. 3). The stain for fat took well (fig. 3*B*). The corneal epithelium appeared normal. Bowman's membrane was present in places and absent in others. Where present, it appeared less refractile than normal. Cellular infiltration and vascularization were present in the anterior two thirds of the stroma. The deeper layers of the substantia propria were less heavily involved. The endothelium and Descemet's membrane were not involved. No fat globules were present in the epithelium. Numerous capillaries, consisting of simple, endothelium-lined tubes, were seen coursing in various directions through the anterior two thirds of the stroma. Prominent around these vessels, especially in the superficial layers, were focal accumulations of macrophages with rare lymphocytes. These were absent in some areas. The lamellae were thickened and not easily identified. Large and small globules of fat were numerous both within the macrophages and, more often extracellularly. These globules were most conspicuous in the deeper portion of the cornea, where the cellular infiltration was least conspicuous. A few fibroblasts were seen in the superficial layers of the stroma. No fatty acid crystals were noted, and polariscopic examination revealed no doubly refractile cholesterol crystals.

Pathologic examination of the tumor removed from the left axilla showed a typical lipoma.

Further Course.—On November 11, one week after discharge, the patient returned for an examination, at which time his condition was the same as on discharge. On December 9 examination of the left eye with the slit lamp showed that the transplant was much more opaque, with several large vascular loops entering it in the middle of the stroma. Most of the opacity was posterior. Vision was limited to perception of moving fingers in this eye. A tiny injected nodule was present under the conjunctiva, at the insertion of the lateral rectus muscle. The patient was not seen again until Jan. 11, 1946, at which time it was found that the nodule close to the insertion of the lateral rectus had increased greatly in size. An unusual change had taken place in the peripheral zone of the cornea and about the transplant. It was definitely clearing. For the first time the iris and pupil could be clearly made out. Examination with the slit lamp showed that the heavy, yellowish white opacity had been replaced, or absorbed, leaving many whitish, flocculent opacities at various depths. The transplant was quite opaque. A dense, yellowish white opacity was present over the posterior portion of the stroma of the transplant, and on it many discrete crystals sparkled under the light. Vision was limited to perception of moving fingers.

The patient was admitted for biopsy or excision of the subconjunctival nodule. Except for the change in his left eye, physical examination showed that his condition was the same. The cholesterol of the blood measured 227 mg. per hundred cubic centimeters. At operation, a firm mass, 10 by 5 by 3 mm., was observed to be securely attached to the sclera just beneath the lower portion of the tendon

of the lateral rectus (fig. 4). It was immovable and rather vascular. It could not be dissected free from the sclera; so, with a keratome, it was removed by sharp dissection flush with the sclera. No foreign body was seen. The lateral rectus was not involved in the mass. The incision was closed with a running black surgical silk suture. The postoperative course was uneventful, and the incision healed well. The suture was removed on the sixth postoperative day.

Ten weeks after operation the mass had not recurred. The excised tissue was fixed in Zenker's fluid. Histologic examination showed a nonspecific granu-

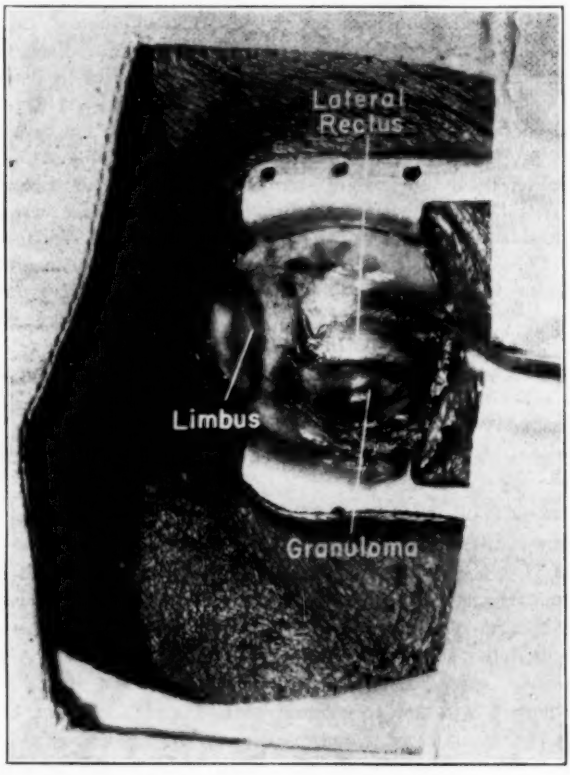

Fig. 4.—Granuloma in the sclera near insertion of the lateral rectus muscle.

lomatous type of inflammatory process with many scattered giant cells. Macrophages, plasma cells and a few lymphocytes were also present. The arrangement was not in accordance to any particularly significant pattern, and no necrosis was present. Stains for acid-fast organisms revealed no tubercle bacilli. No foreign bodies were seen. Stains for fat revealed small globules of fat in some of the macrophages but no foam cells typical of lipidosis. It was impossible to determine the exact nature of the inflammatory reaction, but a foreign body reaction could not be ruled out. The histologic picture was not suggestive of tuberculosis or lipidosis. Material taken from the left conjunctival sac yielded no fungus on culture.

COMMENT

Primary fatty dystrophy has been described as beginning either peripherally or centrally.[17] In the cases of peripheral origin the lesion usually starts as an opacity deep in the stroma close to the limbus. The opacity gradually progresses centrally, although in some cases it has remained stationary while under observation; in still others exacerbations of activity have been associated with symptoms. There is usually a relatively clear zone close to the limbus, although in the deep portions there may be some discrete opacities. The opacity is always heavily vascularized, both by deep-looped vessels and by superficial, dilated and tortuous vessels derived from the conjunctiva.

The central lesions tend to be small and localized, although they may involve the entire cornea except for a clear zone peripherally. After observation of various stages of the condition in the present case, from appearance of the peripheral lesions through the development of the heavy central opacity to the definite clearing of the periphery, it seems plausible that the central lesions may have been a late stage of the peripheral lesion and that all fatty dystrophies follow the same pattern of progression.

Primary fatty degeneration is almost invariably bilateral. A grayish yellow opacity is first observed, which later becomes fibrosed, with yellow masses and whitish plaques visible, in most of the reported cases needle-like crystals being present. The active lesions spread toward the center of the cornea and become more superficial. Apparently, painful symptoms result when the epithelium is involved.

The etiologic factors are obscure. Endocrine disturbances, faulty fat metabolism, hypercholesteremia, circulating toxins, poor diet and repeated minimal trauma have been considered as causative factors.

In 6 of the reported cases of lipid dystrophy blood cholesterol findings were listed. In 3 of the cases values were within normal limits.[18] Two of them were within the upper limits of normal.[19] In the case reported by Meesmann [12] the blood cholesterol was 360 mg. per hundred cubic centimeters. In the case described here the blood cholesterol varied between 390 and 227 mg. per hundred cubic centimeters (normal 250 mg. per hundred cubic centimeters). When, after the second determination, the value was found to be 300 mg. per hundred cubic centimeters, the patient was placed on a low fat, low cholesterol diet. After this diet had been followed for twelve days the blood cholesterol was 250 mg. per hundred cubic centimeters.

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17. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, pp. 2022-2024.

18. Kamocki.[1] Katz and Delaney.[2]

19. Tertsch.[3] Bachstez.[4]

The following biopsy observations were made repeatedly on corneal specimens in these cases:

1. Fatty infiltration occurred throughout the layers of the cornea in varying degrees. The epithelium, Bowman's membrane, the substantia propria and the endothelium were involved, but this deposition of fat was mainly observed in the stroma.

2. Lamellae of the stroma showed degenerative changes and vacuolation.

3. There was infiltration with large mononuclear macrophages the cytoplasm of which was filled with fatty granules. Most of the fat was observed in these cells.

4. Crystals became more prominent as the lesion became older, and as this process proceeded the macrophages became fewer.

5. In most cases more fat was shown with a sudan stain than with an osmic acid stain. Thus, more cholesterol than neutral fat was present.

An interesting problem in cases of this condition is to determine the presence or absence of any ocular inflammation which may be the cause of the lipid dystrophy. Assuredly, primary fatty dystrophy is rare.[20] Heath [21] stated, however, that such an entity does not exist, but that "lipid keratitis," of unknown origin, is always associated with low grade uveitis.

The patient whose case is described here has been followed for twenty-one months, with examinations at intervals of from one week to three months. At no time has any evidence of intraocular inflammation been noted in either eye. As a matter of fact, for over a year, the diagnosis of primary lipid dystrophy was not considered and evidence of inflammation, especially in the left eye, with the more advanced lesions, was sought. There were three periods during which superficial staining was found in the right eye. However, no symptoms were noticeable and the presence of intracellular and extracellular fat globules among the epithelial cells may account for the desquamation of the epithelium.

The nodule that arose from the episclera and sclera in the left eye presents an interesting pathologic problem. Sections cut through various portions of the mass revealed a nonspecific granulomatous type of inflammatory process. A foreign body reaction could not be ruled out. The fact that a black surgical silk traction suture was placed directly through the area from which the granuloma arose, during the corneal transplantation, may explain a foreign body reaction. However, no foreign body was seen at operation or in the specimen.

The reduction of the density of the opacity that occurred at the same time that the nodule developed may represent regular progression of the

20. Duke-Elder.[17] Shapira, T. M.: Am. J. Ophth. **16**:1080, 1943.

21. Heath, P.: Lipin Interstitial Keratitis, Arch. Ophth. **13**:614 (April) 1935.

primary fatty dsytrophy or may have resulted from the increased vascularity caused by the granuloma.

SUMMARY

A case of primary lipid dsytrophy with hypercholesteremia is presented. The patient has been followed for twenty-one months, and the lesion in the left eye has progressed steadily and asymptomatically without evidence of inflammation on examination with the slit lamp.

A corneal transplantation was done on this eye, and pathologic studies of the transplant and of biopsy specimens of the cornea of both eyes revealed marked deposition of fatty globules in both corneas. Doubly refractile cholesterol crystals were seen in the epithelium of the left eye.

After corneal transplantation in the left eye, a granuloma developed in the sclera near the site of insertion of the lateral rectus muscle. It was removed, and pathologic study revealed a nonspecific granulomatous type of inflammatory reaction. This may have been a foreign body reaction, resulting from a suture placed through the site of origin during the operation.

The peripheral zone of the left cornea cleared up considerably at the same time that the nodule developed. It is suggested that this may be coincidental and that it represented the natural course of primary lipid dystrophy.

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ESOTROPIA FOLLOWING OCCLUSION

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IT IS commonly known that temporary loss of vision in one eye may precipitate heterotropia in an infant, but ophthalmologists prescribe monocular occlusion in older children and adults with little concern that persistent esotropia may result. For example, prolonged patching of the better eye is used in the treatment of unilateral amblyopia and prolonged monocular bandaging in the treatment of corneal inflammations. The fact that esotropia has received little attention as a complication of occlusion suggests that it is rare in older children and adults; however, a review of 1,000 cases of esotropia observed in the eye clinics of the State University of Iowa College of Medicine and the University of Oregon Medical School revealed 4 such cases. Medicolegal problems were involved in 3 of the 4 cases; therefore, these cases are reported as representative of a serious, but little known, complication of a standard therapeutic and diagnostic procedure. An analysis of these cases suggests means of preventing and treating the complication.

REPORT OF CASES

CASE 1.—An 8 year old white boy complained of impaired vision in the right eye. Cycloplegic refraction revealed 3 D. of hyperopia and 1 D. of astigmatism in each eye. Visual acuity was 20/20 in the left eye, but the right eye could be corrected to only 20/100. There was no manifest deviation, but postcycloplegic examinations with the Maddox rod and cover tests revealed an esophoria of 6 prism diopters for distant and 9 prism diopters for near fixation. Prism convergence was 12 diopters and prism divergence 3 diopters. The vertical vergences were 2 prism diopters. Ductions were full, and binocular rotations were concomitant when measured with a red and green filter projection system of the type described by Lancaster.[1] The full cycloplegic correction was prescribed. The parents were advised that occlusion of the left eye would be considered after the patient had worn this correction for six weeks; but a few days later the parents became impatient and covered the left lens. When the patch was removed six weeks later, visual acuity in the right eye was improved to 20/70; but the boy described double vision. A concomitant esotropia was present, varying from 7 to 10 degrees for distant fixation and up to 35 degrees for near fixation

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1. Lancaster, W. B.: Detecting, Measuring, Plotting, and Interpreting Ocular Deviations, Arch. Ophth. **22**:867-880 (Nov.) 1939.

(33 cm.). On the major amblyoscope the boy was able to fuse simple targets only when the instrument was adjusted exactly to the angle of the squint. Occlusion was discontinued, but spontaneous recovery did not occur in the ensuing week. Instead, the deviation increased several degrees. Orthoptic exercises were then started.[2] After a month of training with the major amblyoscope and the Remy separator, the boy was again able to maintain single binocular vision for distant fixation; but he was unable to fuse near objects, owing to overconvergence. A 4 mm. recession of the medial rectus muscle of the right eye reduced the deviation to orthophoria. After operation the boy regained comfortable single binocular vision without further orthoptic exercises and remained asymptomatic during the year that he was observed.

In this case the parents assumed responsibility for occluding their child's eye; consequently, there was no medicolegal problem. In the second case, the referring ophthalmologist was responsible for the occlusion and was faced with a malpractice suit.

CASE 2.—A 12 year old white girl had had periodic esotropia, corrected with glasses, at the age of 3 years. She was 11 years old when she first consulted the referring ophthalmologist with a complaint of reading discomfort. At that time corrected visual acuity was 20/100 in the right eye and 20/20 in the left eye. The cycloplegic refractive error was 4 D. of hyperopia in each eye. There was no manifest deviation, but the cover and uncover tests revealed 5 to 7 prism diopters of esophoria for distant fixation. The ophthalmologist advised the parents that there was little hope for restoration of normal visual acuity in the amblyopic eye but stated that there was nothing to lose by occlusion of the better eye. The full cycloplegic correction was prescribed with an occluder over the left eye. When the patch was removed six weeks later, the child described diplopia, and the amblyopic eye was grossly convergent. During the ensuing two months the diplopia gradually disappeared, misleading the family into believing that spontaneous recovery was occurring. Then it became apparent that the deviation would be permanent, and a malpractice suit against the physician was filed. I examined the patient two weeks later.

The patient had a concomitant right esotropia of 15 degrees for distant and of 25 to 40 degrees for near fixation. With a red and green filter projection system, a 15 degree central scotoma could be plotted in the right eye with the left eye fixating.[3] With the major amblyoscope adjusted to the angle of her deviation, the child could fuse simple two dimensional targets over a range of a few degrees. Occlusion of the better eye was resumed to break up suppression, and intensive orthoptic exercises were initiated to increase the amplitude of fusional movements. After two weeks of orthoptic treatment there was no change in the findings; therefore recession of the medial rectus muscle of the right eye was done. Orthoptic training was resumed on the first postoperative day and continued for two weeks before the patient was able to maintain comfortable single binocular vision. Two months after operation measurements with the Maddox rod showed esophoria of 2 prism diopters for distant fixation and 4 prism diopters for near fixation. Prism convergence was 18 diopters and

2. Swan, K. C., and Laughlin, E.: Binocular Orthoptic Training for Amblyopic Patients, Arch. Ophth. **32**:302-303 (Oct.) 1944.

3. Swan, K. C.: Definition of Anomalous Retinal Correspondence, Am. J. Ophth. **28**:58-61 (Jan.) 1945.

prism divergence 4 diopters. The vertical vergences were 1½ prism diopters. Visual acuity in the amblyopic eye had improved to 20/50. The child was able to bar read and had comfortable single binocular vision for the first time in several years. The favorable outcome of the case resulted in withdrawal of legal action against the referring physician.

Profiting by experience with these 2 cases, I have not prescribed prolonged occlusion in the treatment of patients with unilateral amblyopia with single binocular vision. Rather, lacquering of the spectacle lens is used to reduce visual acuity of the better eye to slightly less than that of the amblyopic eye.[4] This procedure permits the patient to maintain peripheral fusion and thereby reduces the danger of converting an esophoria into an esotropia.

The third case differed from the previous two in that occlusion was prescribed for an inflammation of the lids, but an uncorrected refractive error was also an important factor.

CASE 3.—Three months prior to admission, the patient, a 9 year old boy, had received a bee sting on the left upper lid. The eye was rapidly closed by swelling. A week later an abscess on the lid was drained by an ophthalmologist through a superficial incision in the skin. The eye was bandaged and compressed for another week. When the bandages were removed two weeks after the injury, the boy described double vision, and it was noted that his uninjured (right) eye was convergent. The family was advised that spontaneous recovery would occur. During the ensuing two months diplopia gradually disappeared, but the deviation seemed to increase. I then assumed treatment in the case, with the knowledge that a successful outcome was the only means of averting a suit against a fellow ophthalmologist, for the family considered their physician to have been negligent. Examination revealed visual acuity to be 20/30 in the right eye and 20/20 in the left eye. The ductions were full, and binocular rotations were concomitant. The cover test revealed 16 prism diopters of right esotropia for distant fixation and up to 60 prism diopters for near fixation. On the major amblyoscope, with simple disk targets adjusted to the angle of squint, the boy was able to fuse over a range of a few diopters. Cycloplegic refraction revealed 2 D. of hyperopia in the left eye and 4 D. in the right eye. A full correction was prescribed. With glasses, the deviation decreased to 8 prism diopters of convergence, and diplopia recurred. Two weeks of intensive orthoptic training greatly increased the boy's range of fusional movements, but he could not overcome the deviation. Therefore, a recession of the right medial rectus muscle was performed. On the first postoperative day the patient had single binocular vision with stereopsis. Two months later Maddox rod measurements showed orthophoria for distant fixation and 3 prism diopters of esophoria for near fixation. Prism convergence was 20 diopters and prism divergence 6 diopters. The boy was able to bar read. There was no change in the findings one year later. Suit against the referring physician was dropped.

CASE 4.—A white man aged 27 was admitted with a complaint of double vision. He had worn glasses since childhood. Three years previously a cycloplegic refraction by an ophthalmologist had revealed 4½ D. of hyperopia. The full cor-

4. Pugh, M. A.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 913.

rection had been prescribed because the patient had 8 prism diopters of esophoria for distant fixation and 10 prism diopters for near fixation. Prism divergence had been 3 D. and prism convergence 25 D. Four weeks before admission the patient consulted a nonmedical refractionist for a routine examination of his eyes. He was advised that his glasses were too strong and that he had a "latent muscle imbalance." As a diagnostic procedure, monocular occlusion without correcting lenses was prescribed for a week. When the occluder was removed after eight days, the patient had diplopia. This was temporarily relieved by base-out prisms and a small hyperopic correction was prescribed by the refractionist. Then the patient noted a gradually increasing separation of the images. On his admission examination revealed uncorrected visual acuity to be 20/20 in each eye. With cover tests there was a concomitant alternating esotropia measuring 12 to 15 prism diopters for distant fixation and up to 35 prism diopters for near fixation. Single binocular vision could be produced with base-out prisms corresponding to the deviation. On the major amblyoscope the patient could fuse over a range of from 12 to 25 diopters of convergence. Cycloplegic refraction revealed 4½ D. of hyperopia. This correction was prescribed. A week later the patient's deviation had decreased several prism diopters, but he still had periodic diplopia. Daily training was initiated with the major amblyoscope and with the Remy separator. Prism divergence gradually increased up to 3 diopters; then the patient regained comfortable single binocular vision. A suit against the nonmedical refractionist was settled out of court.

COMMENT

It seems probable that prior to occlusion each patient maintained single binocular vision in spite of a strong convergent tendency. A slim reserve of fusional movements, maintained by daily use, was lost when binocular vision was disrupted for a time; however, at least two factors other than a diminished amplitude of fusional movements prevented spontaneous recovery. In the 3 cases in which measurements were obtained, the deviation became considerably greater after occlusion than was indicated by the previously made Maddox rod and cover tests; that is, the convergent tendency was increased by occlusion. It is known that the process involved in fusion exerts some restraint on any tendency of the eyes to deviate from the orthophoric position.[5] This restraint is not completely removed when binocular vision is disrupted for a few minutes, as in the usual clinical tests, but may require several days of occlusion.[6] In addition to diminished fusional movements and an increased deviation, loss of simultaneous binocular perception was another factor which prevented spontaneous recovery of single binocular vision in 2 of the cases. In these cases the response to a diplopia was suppression rather than an increased amplitude of fusional movements.

5. Bielschowsky, A.: Lectures on Motor Anomalies, Hanover, N. H., Dartmouth College Publications, 1940, pp. 11-12.

6. Marlow, F. W.: The Influence of Prolonged Monocular Occlusion in Revealing Errors of the Muscle Balance, Brit. J. Ophth. **4**:145-155 (April) 1920.

Considering these factors, it is evident that spontaneous recovery of single binocular vision is not to be expected in cases of esotropia developing after prolonged monocular occlusion and that prompt treatment would offer a favorable prognosis.

SUMMARY AND CONCLUSIONS

Four cases of esotropia developing during periods of monocular occlusion are reported. Only limited conclusions can be drawn from 4 cases, but it seems that spontaneous recovery of single binocular vision is not to be expected from this uncommon, but serious, complication of a commonly used procedure. Treatment should be immediate; otherwise the deviation tends to increase and the amplitude of fusional movements to decrease, and suppression is likely to develop.

A latent convergent tendency seems to be the condition underlying development of esotropia from occlusion; therefore, in the presence of esophoria or uncorrected hyperopia prolonged monocular occlusion for diagnostic or therapeutic purposes should be used with caution. In the treatment of unilateral amblyopia in patients having single binocular vision, lacquering the spectacle lens to reduce visual acuity in the better eye is suggested as safer than total occlusion because binocular vision is maintained.

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ABSTRACT OF DISCUSSION

Dr. Peter C. Kronfeld, Chicago: In the 4 cases on which Dr. Swan's paper is based, the patients were young hyperopic persons in whom occurred the striking phenomenon of moderate esophoria turning into pronounced esotropia during a period of monocular occlusion. That malpractice suits were filed in 3 of the 4 cases is indicative primarily of the gross change in the patient's appearance and visual comfort which were brought about by the occlusion, and only to a lesser degree of lack of good will on the part of the patient or his parents.

The phenomenon of esotropia following occlusion, as it occurred in Dr. Swan's 4 cases, can be broken down into two "subphenomena," namely, (1) impairment in the patient's ability to produce corrective fusional vergence impulses and (2) an increased, constant convergence impulse. The occurrence of the first subphenomenon after occlusion is thoroughly understandable and well known. The second subphenomenon is an interesting and new phenomenon. Observations in a large number of cases of esotropia and unilateral amblyopia, which is treated by occlusion of the better eye, do not indicate any consistent tendency toward an increased convergence impulse during the occlusion. Variations in the angle of squint occur in these cases, but they are not consistently in the direction of increased convergence. Thus, it would not be correct to say that monocular occlusion in cases of esotropia is conducive to an increase in the angle of squint.

In addition to the quantitative change, that is, the increase in the deviation as found by the cover test, a qualitative change occurred in Dr. Swan's 4 cases. Originally the patients exhibited a noncharacteristic esophoria, whereas after the occlusion the neuromuscular condition was that of a convergence excess.

Proceeding from the simple and common to the complicated and unusual, Dr. Swan's cases may be arranged in the sequence 4, 3, and 1 and 2, with the last 2 cases on the same level. The development of frank esotropia in case 4 is not surprising. A young person with esophoria and 4.5 D. of hyperopia in each eye who has worn his spherical correction for a number of years and is suddenly deprived of it produces stronger accommodative impulses than normally. These are coupled with stronger convergence impulses. This overconvergence does not cause symptoms until the occluder is removed and the patient tries to resume the normal sensorial relationship of his eyes. Inefficiency of the mechanism of accommodation innervation under the unfamiliar conditions of seeing without glasses may account for the increase in the deviation. The patient's favorable response to proper glasses and orthoptic training is readily understandable. I cannot understand why the nonmedical refractionist instituted occlusion therapy in this case.

Case 3 is similar to case 4 except that glasses had never been worn. The patient had maintained binocular single vision by corrective fusional divergence impulses until the monocular occlusion necessitated by an inflammatory disease of the lids dealt a severe blow to the mechanism concerned with the corrective fusional movements. The fact that the patient was now forced to use exclusively, and without the aid of glasses, the eye with 4 D. of hyperopia probably caused abnormal convergence impulses, resulting in a manifest and constant deviation. The occurrence of esotropia under such conditions is one of the many risks that are entailed in the practice of ophthalmology. I vaguely remember a reference to this situation in one of the older manuals on ocular therapeutics, the author recommending a routine phoria test before subjecting any eye to patching. Unfortunately, the state of inflammation and photophobia present in many of these situations makes phoria tests difficult and unreliable.

Cases 1 and 2 were characterized by the presence of unilateral amblyopia and parallelism under conditions of distance fixation. This parallelism was brought about and maintained by corrective vergence impulses originating from eccentric retinal areas. Such sensorial relationships between the two eyes are more easily disrupted than normal ones. The increased state of convergence can probably be explained again by the inefficiency and "awkwardness" of the amblyopic eye.

From the study of the paper, I got the impression that operation was resorted to in order to terminate an embarrassing situation. Theoretically, one would expect a favorable response of this form of esotropia to prolonged conservative treatment. It is remarkable that the recessions performed in 3 of the 4 cases corrected the convergence excess so beautifully and completely.

This is an interesting and stimulating paper.

Dr. George N. Hosford, San Francisco: We are indebted to Dr. Swan for collecting, analyzing and bringing to our attention a group of cases which, fortunately, are not numerous, but certainly are troublesome.

At one time I used monocular occlusion extensively as a diagnostic procedure and in the treatment of amblyopia, and that I have no similar cases to report is due not to any precaution or forethought on my part but purely to good luck. Since I came under the influence of the teachings of the late Dr. James White, I have used monocular occlusion but rarely for diagnosis and do not now believe that that procedure can tell the examiner anything about a patient which he cannot learn without it by other, more rapid and less troublesome, methods. Furthermore, in observing the results of ophthalmologists who do use and rely on it I have found that it is misleading, particularly in cases of double hyperphoria, unless one eye is occluded until it reaches a stable point, after which the patient must be left without occlusion and the eyes given time to return to the usual relationship of position. The other eye must then be occluded until the hyperphoria ceases to increase under the cover. Even with this tedious routine, the data obtained are difficult to interpret (if they mean anything at all); so no great harm will be done if the occlusion test is allowed to fall into disuse.

Corneal lesions present a different problem, as there is no adequate substitute for bandaging in cases of this type, but one must be on the lookout for the possibility of turning a phoria into a tropia. In the rare cases in which this possibility exists, perhaps the bandage could be left off for an hour or two daily. If one should have the misfortune to precipitate a tropia, one obviously should not temporize, but should at once institute adequate treatment, including surgical procedures if necessary.

Dr. Joseph Pascal, New York: Dr. Swan's paper brings up an extremely important point for the reason that it is the general impression in ophthalmology that monocular occlusion can do some good and never any harm. The fact that it may do harm is an important point to consider.

Without analyzing the cases, I think that these patients must have had poor or a subnormal fusion faculty. The use of lacquer in monocular occlusion, covering up the lens of the better eye, is excellent. But in cases in which monocular occlusion is used to develop function in the amblyopic eye, a combined procedure is more desirable—one by which the patient comes to the office for binocular fusional treatment, say every two days or every day, and at the same time is made to use the amblyopic eye monocularly over a period of time. I know that the main objection to prolonged ocular occlusion for diagnostic purposes, as Marlow suggested, has been that this procedure is hard on the patient, but the possibility of such an occurrence as the development of esotropia with diplopia or suppression has rarely been mentioned. The paper is a revelation to me and, I think, to many other men.

Dr. Kenneth C. Swan, Portland, Ore.: Dr. Kronfeld is correct about the reasons for suit. In 2 of the cases legal action was dropped when a successful outcome was assured.

One is impressed with the multiplicity of factors in every case of squint. There is no question that a disturbance of accommodative convergence mechanism was important in these cases, but one cannot be certain that it was the single predisposing factor.

It was striking that before occlusion there was little difference in the amount of latent deviation for distance and near fixation. After occlusion, there was excessive converence with accommodation. This is an indication that the latter condition was of functional origin and therefore not a surgical problem. The deviation for distant fixation is corrected by operation, so that the patient is able to maintain single binocular vision and thereby exercise fusional movements by normal use. As amplitude is gained by normal use and orthoptic training, the functional overconvergence for near fixation decreases, and single binocular vision for near fixation is reestablished.

I have been unable to find references to squint following occlusion, but I agree with Dr. Kronfeld that cases must exist, for the literature contains warnings against the prolonged use of occlusion in the presence of esophoria.

Since the notice of this paper appeared, a few weeks ago, five ophthalmologists have advised me that they have observed similar cases in their private practice. I believe that the development of esotropia after occlusion is more common than the literature has led one to believe, for a physician is hesitant about reporting cases which may involve him in legal action.

PENTOTHAL SODIUM IN OPHTHALMIC SURGERY

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AND
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IN THE past decade intravenous anesthesia has shown a definite and consistent increase in its application and use. We feel that this form of anesthesia has a definite place in ophthalmic surgery for the following reasons:

1. The technic of administration is simple.
2. The period of induction is short and pleasant.
3. The usual psychic shock is absent.
4. The depth of narcosis is controllable and sufficient for any ophthalmic procedure.
5. The administration may be repeated without danger of becoming habit forming.
6. The operative field is free of the anesthetist and his equipment.
7. The intraocular tension is reduced 40 to 60 per cent.

We do not advocate intravenous anesthesia for all types of ophthalmic patients. We wish to emphasize that the contraindications to the intravenous use of anesthetic agents must be observed. Children under 7 or 8 years of age, unless robust, are poor subjects. In addition to their natural fear and small veins, the inertia of the air and their narrow air passages hinder gaseous exchange and create an undesirable situation in view of their relatively high oxygen requirement. Such patients do very well under anesthesia induced with solution of tribromoethanol U.S.P. and ether, since the former prevents psychic shock, which children frequently show during the induction period.

THE AGENT OF CHOICE

In a study of several anesthetics for intravenous use, we found pentothal sodium to have the following advantages over other agents: 1. It is equally, if not more, powerful and rapid in action. 2. Twitching is

Read at the meeting of the Pittsburgh Ophthalmological Society Nov. 26, 1945.

From the Department of Anesthesiology (Dr. Thomas) and the Department of Ophthalmology (Dr. McCaslin), University of Pittsburgh School of Medicine, the Eye, Ear, Nose and Throat Hospital and St. Francis Hospital.

rare. 3. Postanesthetic nausea and vomiting are less frequent. 4. Relaxation is more satisfactory. 5. Recovery is more rapid.

The data presented today are based on 3,050 administrations of pentothal sodium for all types of ophthalmic surgery. The youngest patient was 7 years and the oldest 93 years of age.

The amount of pentothal sodium used ranged from 3 to 45 grains (0.195 to 2.925 Gm.). The duration of anesthesia extended from three to ninety-five minutes. There were several patients who received repeated administrations within a short space of time, without ill effects. We have administered pentothal sodium without serious results to several patients with coronary heart disease, several with bundle branch block and 2 with infarct in the ventricular septum.

We are of the opinion that our good fortune may be attributed to the technic of administration and to the management of these patients during anesthesia and during recovery from the anesthetic.

TECHNIC OF ADMINISTRATION

Administration of Pentothal.—We shall not describe all the details of the administration of pentothal, since this is solely a problem for the anesthetist. However, we wish to discuss in detail the preanesthetic preparation of the patient, some important steps in the administration of the anesthetic and the management of patients to be operated on for cataract. We shall describe the procedure used for such an operation because this must be flawless, since a simple error may result in the loss of an eye. This technic, however, is applicable to all types of ophthalmic operations.

THE TECHNIC IN DETAIL

1. The patient should be in the hospital at least one day before operation.

2. An enema should be given eight to twelve hours before operation.

3. A hypnotic, preferably pentobarbital, should be given the night before operation, to determine the patient's idiosyncrasy to barbiturates and to provide a restful night.

4. Sips of water are permitted until two hours before operation.

5. A preoperative hypodermic, the usual dose of morphine and atropine sulfate, is sufficient, and proper preoperative medication is essential for smooth pentothal anesthesia. Opiates are used. The necessity for the use of atropine should be emphasized. These preoperative agents control the parasympathetic hyperactivity and inhibit salivary and mucous secretions, thereby greatly reducing the incidence of complications such as coughing, sneezing and laryngospasm. The preoperative medicament should be administered hypodermically forty-five minutes before injections of the anesthetic.

6. Two drops of 4 per cent cocaine hydrochloride should be instilled in each eye thirty minutes before the scheduled time of operation. This will aid in preventing sneezing.

7. Instillations of cocaine should be continued in each eye every ten minutes before the patient goes to operation and repeated on his arrival in the operating room.

8. Instillations of cocaine are again repeated just before the preparation of the eye for operation.

9. In order to maintain a minimal dose of pentothal, we request the surgeon or the assistant to check over the instruments and prepare the sutures necessary for the operation before the anesthesia is started.

10. The venipuncture is made just as the patient is being prepared for the operation.

11. We have been using a 4 per cent solution of pentothal sodium for patients under 50 years of age and a 2 per cent solution for those who are 50 and older. One and one-half cubic centimeters of nikethamide is added to each gram of pentothal sodium for the latter group and for patients with a history of coronary disease or arteriosclerosis, in the belief that the nikethamide will dilate the coronary vessels, thereby increasing the oxygen supply and nourishment to the heart.

12. Pentothal is started in the usual manner and with the customary care. Three cubic centimeters of the solution is injected during a period of eight to ten seconds. Because relaxation comes on more slowly than unconsciousness, it is important that a pause of five seconds follow the injection of each 2 or 3 cc. of the agent. An additional 2 or 3 cc. is injected at the same rate as at the beginning, followed by another pause of five seconds. This procedure is continued until the desired plane of anesthesia is obtained.

13. To prevent or to correct mechanical obstruction we avoid using the oropharyngeal airway, for fear of causing laryngospasm. To prevent mechanical obstruction, we have used a tongue suture. If the tongue suture is inserted properly, there should be no bleeding, and the patient should have no discomfort when consciousness returns.

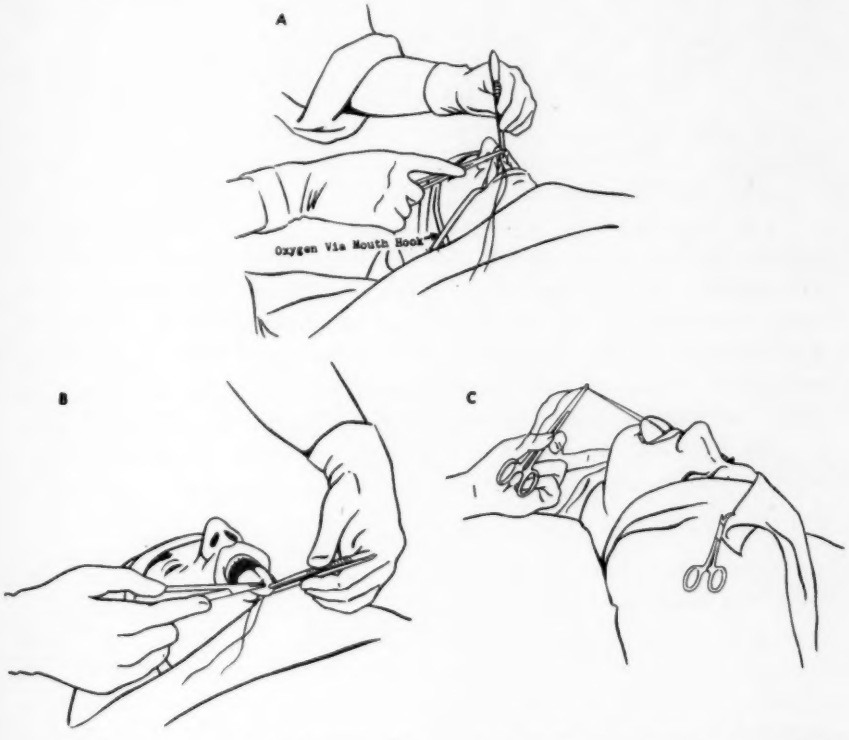
The technic of insertion of the tongue suture is as follows: The tongue is grasped with a thumb forceps and pulled forward and upward. The needle and the suture are inserted 1 fingerbreadth from the tip of the tongue, in the center and between the lingual vessels, as illustrated in *A* of the figure.

The second step is illustrated in *B*. The tongue is pulled forward and downward, and the needle and the suture are pulled through. The needle is removed from the suture.

The third step is illustrated in *C*. The ends of the suture are held with a forceps, and the mandible is supported in the manner illustrated.

It is important to support the mandible in order to obtain a patent airway. Furthermore, one must remember that too severe tugging on the tongue will result in great discomfort for forty-eight hours after operation.

14. Oxygen is administered through a mouth hook when the patient is in deep analgesia or in light anesthesia, as illustrated in *A* of the figure. Good color is of prime importance. A patent airway is of most importance.



Steps in insertion of the tongue suture. *A*, first step. The tongue is pulled forward and upward, and the needle and suture are inserted 1 fingerbreadth from the tip of the tongue, in the center and between the lingual vessels. *B*, second step. The tongue is pulled forward and downward, and the needle and suture are pulled through in the manner illustrated. *C*, third step. The suture is held with a forceps, and the mandible is supported in the manner illustrated.

15. The plane of anesthesia may be determined by the three reflexes: (*a*) when the lid retractor is inserted (lid reflex); (*b*) when the superior rectus muscle suture retractor is inserted, and (*c*) when iridectomy is done. At this stage of the operation the patient should be in the proper plane of anesthesia for the section and the cataract extraction.

16. During the section and cataract extraction, slow injection of 0.5 cc. of the pentothal solution is made, with a twenty second pause following each injection.

17. One cubic centimeter of the pentothal solution is given when the cataract is delivered. The needle is removed from the vein when the dressings are applied to the eyes.

18. The person who returns the patient to the room instructs the nurses to place a pillow under the head and shoulders, raise the back rest of the bed one notch, give oxygen with a mouth hook and make certain that the patient has a patent airway at all times.

The O'Brien [1] block may be performed after preparing the eye for operation. We prefer this procedure because it adds another precaution in cataract surgery. This block prevents squeezing of the lids and consequent loss of vitreous should the patient be in too light a plane of anesthesia. The technic is as follows:

A 1 inch (2.5 cm.) needle, 25 gage, is inserted through the skin and tissues 1 fingerbreadth in front of the tragus of the ear and directed downward to the anterior part of the condyle of the mandible. One cubic centimeter of 2 per cent procaine hydrochloride is injected. The needle is slowly withdrawn and at the same time another cubic centimeter of the procaine is infiltrated into the tissues. With the thumb or index finger, pressure is applied over the infiltrated area. In two or three minutes the transitory paralysis of the orbicularis oculi muscle begins; this wears off in less than one hour.

COMPLICATIONS AND THEIR MANAGEMENT

Complications with pentothal anesthesia are rare. However, some occur and should be managed without serious results. The most common is respiratory depression. The amplitude of the respiration, rather than the rate, is affected. We have found that oxygen administered through a mask, a catheter or a mouth hook is frequently sufficient to provide good color.

Other complications which may occur either in deep or in light anesthesia are coughing, laryngospasm and hiccup. These may cause alarming cyanosis and perhaps cardiac embarrassment if persistent. Such complications are undoubtedly due to parasympathetic hyperactivity. If they occur when the patient is under anesthesia, we aspirate the mucus or other material in the pharynx, deepen the anesthesia and immediately increase the flow of oxygen.

Trismus is another complication. This is undoubtedly a result of parasympathetic hyperactivity, which can be controlled with atropine.

1. O'Brien, C. S.: Akinesis During Cataract Extraction, Arch. Ophth. **1**: 447-449 (April) 1929.

Should this occur during anesthesia, a nasopharyngeal tube should immediately be inserted and oxygen administered under pressure. Delay in this procedure may be serious.

POSTANESTHETIC COMPLICATIONS AND THEIR MANAGEMENT

The most common postanesthetic complication is respiratory depression. For this reason, all patients anesthetized with pentothal should have oxygen administered to them continuously after the operation until they have completely reacted. Furthermore, the entire nursing staff of all hospitals should be thoroughly trained in the proper management of patients receiving barbiturates. The nursing staff should be made to realize that the postoperative and postanesthetic care of patients is very important for uneventful recovery.

Postanesthetic opiates should be withheld, especially in the case of older persons, until the patient has completely reacted from the anesthetic.

If a patient has not reacted within two or three hours, it means that an overdose of pentothal has been administered. In this case treatment is as follows:

1. The patient is kept warm.
2. Oxygen is administered continuously.
3. The mucus is aspirated from the throat frequently.
4. Metrazol, 3 cc., is given intravenously. The injection is repeated in five minutes if necessary. (Incidentally, it has been found that metrazol is an efficient denarcotizing agent, as well as an excellent respiratory stimulant, if given in a sufficient dose.)
5. Hypertonic solution of sucrose is given intravenously for diuresis and dehydration of the brain and the lungs.
6. Repeated small transfusions of plasma are helpful.

CONTRAINDICATIONS

Pentothal sodium should not be employed or recommended when there is pronounced physiologic or mechanical interference with the respiratory function. It is contraindicated with inflammatory conditions of the neck complicated by edema of the glottis and with tumors of the neck encroaching on the glottis and interfering with respiration. Children under 7 or 8 years of age, unless robust, are poor subjects. It is inadvisable to use this agent with patients who have respiratory embarrassment due to cardiac decompensation. We feel that pentothal is contraindicated in the presence of bronchiectasis, severe anemia and shock.

CONCLUSIONS

A brief review of the technic of pentothal sodium anesthesia in ophthalmic surgery is presented, with special attention to the complications and their management, and to the contraindications. Pentothal is not a drug with which liberties may be taken. Special care should be exercised in maintaining an efficient airway at all times. A gas machine should always be on hand and ready for use should respiratory depression or other complications present themselves. Finally, the drug should be administered by a thoroughly trained anesthetist, who is competent to deal with any situation that may occur during the administration of this popular, but potent, agent.

Dr. John C. Dunbar photographed the various steps in the development of this technic.

4066 Penn Avenue.

OPTOKINETIC AND OTHER FACTORS MODIFYING VESTIBULAR NYSTAGMUS

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IT HAS been common practice clinically to concentrate attention in ophthalmologic diagnosis on the two separate entities of "ocular" and "central" nystagmus. In so doing, optokinetic nystagmus has been relegated to a group of interesting phenomena which have little application in practice. The purpose of this paper is to present the accumulated knowledge regarding the modifying effect of optokinetic nystagmus and to add further experimental data.

Optokinetic nystagmus has been typified in ophthalmologic literature by the term "railroad nystagmus." When a subject allows his gaze to follow a moving object in the passing landscape, a slow deviation occurs which allows fixation to be maintained on the object. When an end position is reached beyond which head movement would be required for further fixation, a quick return to the primary position occurs, and the cycle is repeated as long as attention is maintained. The slow and quick components of the nystagmus thus are related to the direction of movement of passing objects and present the same relationship to each other as do the components of ocular motion produced by vestibular stimulation. Moving objects passing from left to right elicit a nystagmus identical with that observed by rotating a subject to the left, and vice versa.

Evidence of the close interrelationship of optokinetic and vestibular nystagmus has been steadily accumulating through the past several decades. Unfortunately, however, clinical practice and medical teaching have failed to keep pace adequately with the experimental findings. The usual concept which is presented to the student is that the nystagmus induced by rotation is purely a vestibular phenomenon. This is true only to the extent that angular acceleration (change in speed of turning) produces rotational response and angular deceleration elicits postrotational effects. Extensive modifications of response can be produced by many other factors, chief among which is the optokinetic nystagmus also produced by rotation.

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		10	8T	10	+	0	+	0	+	0	3T	11	4T	6	4T	10	8½T	0
		20	6T	12	+	0	+	0	+	0	3T	10	4T	4	4T	7	3½T	0
2	½	1	?	0	+	0	+	2	+	0	+	0	+	0	+	0	+	0
		5	0	2	Sl	5	+	9	?	7	+	3	+	10	+	1	+	1
		10	+	31	Sl	18	+	17	?	15	+	25	+	17	+	0	+	11
	¼	1	+	0	+	0	+	0	0	3	+	0	+	2	+	0	+	1
		5	+	0	+	5	Sl	10	0	5	+	9	4T	5	+	3	+	5
		10	8T	22	9T	7	+ → Sl	9	0	5	6T	10	4T	6	5T	7	±	8T
		20	10T	19	10T	9	5T	11	3T	7	6T	11	4T	5	1T	9	0	7T
4	½	1	+	0	+	0	0	0	+	0	+	0	+	0	+	0	+	0
		5	+	8	+	3	Late	0	+	3	+	6	+	6	+	0	+	1
		10	+	12	+	4	+	18	+	45	+	29	+	42	+	2	+	5
	¼	1	+	0	+	0	+	0	+	4	+	0	+	0	+	0	+	1
		5	+	2	+	0	+ → ±	16	+	14	+	8	+	9	+	0	+	10
		10	+	0	+	0	5T	15	3T	17	8T	15	7T	7	+	5	6T	15T
		20	+	0	+	0	5T	13	3T	10	8T	13	8-9T	6	8T	15	8T	12T
5	½	1	+	0	+	1?	+	0	+	0	+	0	+	0	+	0	+	0
		5	+	3	+	3	+ → 0	7	+	3	+	4	+	2	+	0	+	0
		10	+	11	+	5	+ → 0	57	+	30	+	16	+	7	+	5	+	1
	¼	1	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0
		5	+	5	+	0	+	8	+	0	+	2	+	0	+	7	+	0
		10	+	7	+	0	9T±	15	+	0	+	7	+	0	0	7	+	0
		20	9T	8	+	0	11T	8	+	0	12T	8	16T	9	1T	7	1T	0
6	½	1	+	0	+	0	+	0	+	1	+	0	+	0	+	1	+	1
		5	+	4	+	3	0 → +	2	+	0	+	1	+	1?	+	0	+	0
		10	+	6	+	2	+	1	+	6	+	0	+	6	+	0	+	0
	¼	1	+	0	+	0	+	0	+	0	+	0	+	0	+	1	+	0
		5	+	0	+	0	+	0	+	4	+	0	+	0	+	1	+	0
		10	+	0	+	1?	+	0	+	5	+	0	6T	6	9T	3	4½T	0
		20	+	0	+	0	+	0	4T	4	+	0	8T	7	6T	6	3T	0
7	½	1	0	0	+	0	0	2	0	0	+	0	+	0	+	0	+	1
		5	Sl	17	+	3	0	7	0	3	+	5	+	1	+	2	+	1
		10	Sl	23	+	11	0	18	+ Late	13	+	8	+	3	+	2	+	12
	¼	1	0	0	+	0	0	2	0	0	+	0	+	0	+	0	+	0
		5	+	14	+	0	0?	9	Late	4	+	0	+	0	+	0	+	0
		10	Sl	12	+	0	+ → 0	7	7T	6	+	0	+	0	+	0	+	12
		20	3T	11	12T	8	+ → 0	7	7T	6	+	10†	+	0	+	1	0	5

* In this table, Sl indicates slight nystagmus; Rot, rotational nystagmus; PR, postrotational nystagmus; +, nystagmus present throughout rotation, and T (with numeral), number of turns to which rotational nystagmus persisted.

† Components reversed.

‡ ½ means 1 turn per two seconds; ¼ means 1 turn per four seconds.

	5			6				7				8 Not Blindfolded				Blindfolded	
	To Right		To Left	To Right		To Left		To Right		To Left		To Right		To Left			
	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Right PR	Left PR
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	0	+	14	+	7	+	0	+	0		
7½T	0	+	0	+	0	+	0	0	50	+ → ±	29	+	0	+	0	11	11
+	0	+	0	+	0	+	0	+	1	+	4	+	0	+	0		
+	0	+	0	+	0	+	0	+ Sl	18	2T	12	+	0	+	0		
2½T	0	+	0	+	0	+	0	4T	19	2T	7	+	0	+	0		
2½T	0	+	0	+	0	+	0	3T	16	2T	11	+	0	+	0	5	5
+	0	+	0	+	0	+	1	+	1	+	0	+	0	+	0		
+	1	?	4	+	2	? Sl	6	+	2	+	5	+	0	+	1		
+	11	+	10	+	7	Sl	10	+ → ±	10	6T	11	2T	6	2T	7	12	12
+	1	+	1	+	1	Sl	2	+	1	+	3	+	0	+	0		
+	5	3T	4	+	4	Sl → 4T	3	2T	6	2T	4	4T	7	+	0		
±	8	3T	4	6T	7	Sl → 3T	4	3T	8	2T	5	4½T	6	4T	5		
0	7	3T	5	5T	6	Sl → 2T	3	3T	8	2T	6	4T	6	4T	5	9	7
+	0	+	0	+	0	+	0	+	1	+	1	+	0	+	0		
+	1	+	1	+	0	+	0	+	17	+	12	+	0	+	0		
+	5	+	1	+	20	+	13	7 T	62	6	32	+	0	+	6	17	22
+	1	+	0	+	2	+	0	+	11	+	6	+	0	+	0		
+	10	+	0	3T	14	+	0	3T	12	2T	13	+	0	+	0		
4T	15	+	0	3T	7	+	0	2T	17	1T	16	+	0	+	0		
5T	12	+	0	2T	16	16-18T	15	3	17	1T	13	+	0	7½T	4	9	7
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	1	+	0	+	0	+	0	+	0	+	0	+	0		
+	1	+	1	+	1	+	+	+	0	+	1	+	0	+	2	20	16
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	2	+	0	+	0	+	0	9T	0	+	0		
18T	0	+	0	+	0	+	0	+	0	+	0	9T	0	+	0	9	10
+	1	+	0	+	1	+	0	+	2	+	0	+	1	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0	21	15
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
4½T	0	+	0	+	0	+	1	+	0	+	0	+	0	+	0		
5T	0	+	0	+	0	16T	4	+	0	+	0	+	0	+	0	8	5
+	1	+	0	+	0	+	0	+	0	+	1	+	0	+	0		
+	1	+	1	+	2†	+	1	+	0	+	1	+	1	+	0		
+	12†	+	2	+	4†	+	1	+ → ±	13	+	3	+	2	+	3	16	14
+	0	+	0	+	0	+	1†	+	4	+	0	+	0	+	0		
+	0	+	1	+	0	+	1†	1T	10	+	0	+	0	+	0		
+	13†	+	0	+	1†	+	1†	0?	8	+	0	+	0	+	0		
0	5†	+	1†	+	2†	+	0	0?	8	+	0	+	3†	+	0	2+	8

Experiments had been performed by many workers demonstrating such modification, but it remained for Mowrer [1] adequately to analyze and correlate experimentally the interrelationship in the pigeon, and to some extent in man. He noted that the nystagmus present after rotation could be completely inhibited by the optokinetic nystagmus occurring during rotation and stated that this was due in part to a persistence of the optokinetic response which carried over into the postrotational period. This finding has been confirmed by my experiments.

Domestic white rabbits were utilized for our work, both because of their use in previously reported experiments and because of ease of procurement and handling. A series of 6 young males was subjected to repeated daily rotation in the horizontal plane with vision permitted during the tests. A hand-turned rotational table was used, with the animal's head fixed in a Czermak holder. Each animal was rotated through one, five and ten turns to the right, at a rate of one turn in two seconds, then through one, five, ten and twenty turns, at a rate of one turn in four seconds. This entire procedure was then repeated with rotation to the left. A rest period of approximately thirty seconds was allowed after each rotation. Postrotational nystagmus was recorded by visualizing the number of movements of the eyes occurring after deceleration. Rotational nystagmus was noted only as to its presence or absence.

The table presents the findings. If rotational nystagmus persisted throughout the period of rotation, it was designated by a plus sign (+). If it ceased during rotation, the number of turns through which it persisted was noted (e. g., 3 T). Postrotational nystagmus was recorded numerically as the total of "beats" of nystagmus seen. At the end of eight consecutive days of rotation, the animals were blindfolded, and rotation was performed through ten turns at the faster rate and through twenty turns at the slower rate. This was done both to the left and to the right. The blindfold was quickly removed at the end of each rotation and the postrotational nystagmus observed. This is recorded in the last two columns of the table.

Certain facts become evident from examination of the recorded results. In all instances there was a definite reduction in the amount of postrotational nystagmus occurring when the animals were repeatedly rotated with vision permitted. The reduction was finally complete in the majority of instances, but it diminished at different rates in different subjects. In all cases postrotational nystagmus was present after blindfolded rotation of the animals at the end of the series of rotations. An example of these findings is presented graphically in chart 1. If rotational nystagmus was maintained throughout the period of turning, the postrotational response was consistently less. Toward the end of the series, if nystagmus was maintained in the animal throughout rotation,

1. Mowrer, O. H.: (*a*) The Modification of Vestibular Nystagmus by Means of Repeated Elicitation, Comparative Psychology Monographs, Baltimore, Johns Hopkins Press, 1934, vol. 9, no. 5; (*b*) Influence of Vision During Bodily Rotation upon the Duration of Post-Rotational Vestibular Nystagmus, Acta otolaryng. **25**:351-363, 1937.

the postrotational response was abolished, with few exceptions. If rotational nystagmus failed, the postrotational response was present to a greater extent and reached a level directly proportional to the number of turns through which the rotational response persisted.

After blindfolded rotation there was not a uniform correlation of response with the original postrotational nystagmus. However, those animals which had a relatively poorer postrotational nystagmus at the beginning had an even greater blindfolded response (animals 4, 5 and 6, table). It was noted also that in these subjects nystagmus was better maintained throughout rotation on the first day. However, those animals with a more marked postrotational response at the start of the series in general presented a blindfolded response which was less than

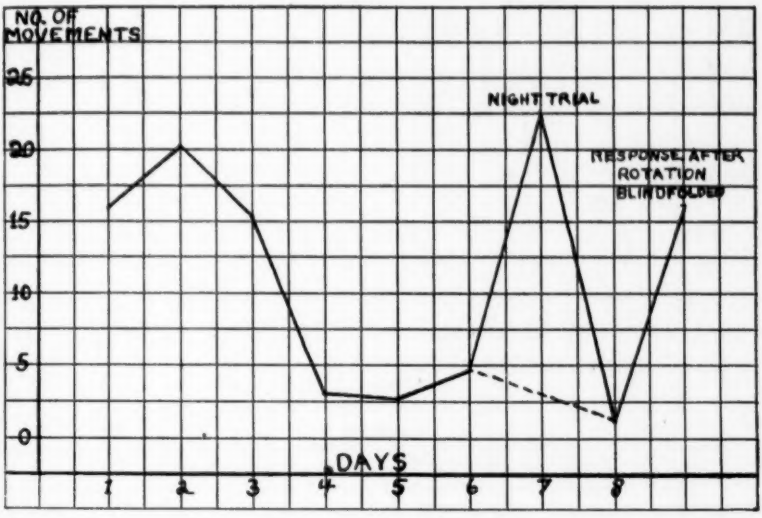

Chart 1.—Average amount of postrotational nystagmus in all subjects after ten turns to the right in twenty seconds.

that originally seen (animals 1, 2 and 7, table). Nystagmus was not maintained so well in the latter subjects throughout the rotation on the first day.

On the seventh consecutive day of rotation of the nonblindfolded animals, several of them demonstrated a greater amount of postrotational response than had been noted on previous days. This day's tests were performed late in the evening, after the rabbits had been in the dark for several hours, and all other tests were done in the afternoon. It was uniformly noted that those animals with greater responses were those which appeared more sleepy and less in contact with their environment. The following day all these subjects returned to their previous levels of reduction (chart 1, night trial). An example of the results with

rabbits 5 and 6, which failed to show an increase in response on the seventh day, is presented in chart 2. The latter subjects were wide awake and alert during the tests.

In 1 subject only (animal 7) an actual "reversal" of the expected postrotational response occurred. Here, the slow and quick components of the rotational nystagmus persisted after rotation, instead of showing a transposition of their components, such as was usually seen. These instances are marked by a dagger in the table.

Reduction of postrotational response has been variously interpreted by different workers. Hoshino [2] found a reduction on repeated rotation

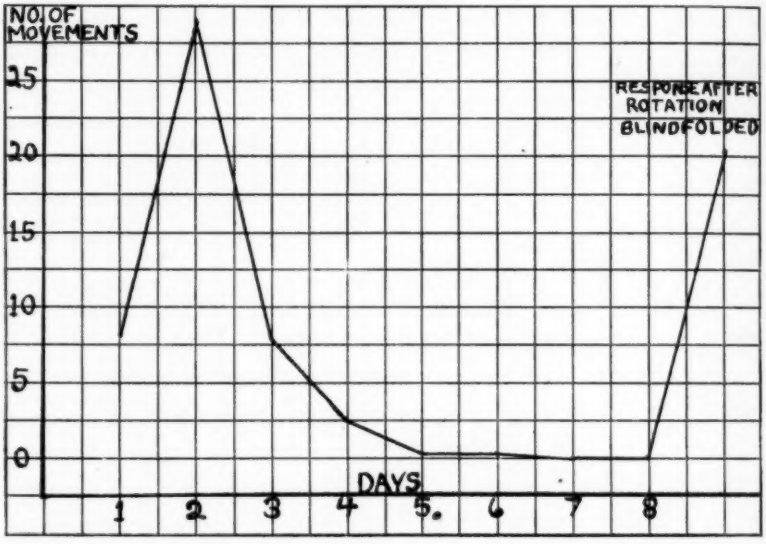

Chart 2.—Average amount of postrotational nystagmus in rabbits 5 and 6 after ten turns to the right in twenty seconds.

in rabbits. Maxwell, Burke and Reston [3] discovered a gradual decrease of postrotational response in rabbits on daily repeated rotation and claimed "habituation" of the animals to be the cause rather than vestibular damage. They also found an even more marked decrease when the animal's head was free rather than fixed. Pilz,[4] continuing with the

2. Hoshino, T.: Vestibuläre Reflexbewegungen des Auges beim normalen Kaninchen, Acta oto-laryng. **4**:328-338, 1922.

3. Maxwell, S. S.; Burke, V. L., and Reston, C.: The Effect of Repeated Rotation on the Duration of After-Nystagmus in the Rabbit, Am. J. Physiol. (March) 1924.

4. Pilz, G. F.: On the Relation of After-Nystagmus to Rotation-Nystagmus; Direct Effects of Rotation, Am. J. Physiol. **77**:428-442 and 443-458 (July) 1926.

work reported by Maxwell,[5] found that both the rotational and the postrotational nystagmus were reduced by repeated rotation. The postrotational response was decreased more readily, even to obliteration, although the rotational nystagmus was never completely lost. He also felt that retinal modification of labyrinthine effects occurred in the rabbit but that it was of low magnitude. Reports of reduction of postrotational nystagmus in man have been presented by several workers, namely, Griffith,[6] Holsopple,[7] Dunlap[8] and Dodge.[9] The problem has been ably reviewed by Mowrer,[10] and important contributions to the subject were made by him.

Mowrer used pigeons for his experimental work and investigated thoroughly the relationship of visual effects to vestibular responses. He concluded that three factors were operative in reducing postrotational nystagmus. He cited first the tendency on the part of the subject to fixate the visual environment after rotation. Second, in the pigeon, with the head free and with head nystagmus occurring, the continued reversal of vestibular stimulation produced by the head movement made the final deceleration stimulus at the end of rotation less effective in producing vestibular response. Third, he demonstrated a "post-stimulus persistence" of the visually induced rotational nystagmus which carried over after deceleration to inhibit further the postrotational vestibular response. Presumably, the first and third factors were active in reducing postrotational response in our series, but the second factor was eliminated because the rabbits' heads were fixed during the tests.

The influence of fixation on the results obtained may extend even further than by merely acting to inhibit postrotational response. If one considers that the initial rotational nystagmus is due to angular acceleration acting on the vestibular receptors, then this impulse should die

5. Maxwell, S. S.: The Effect of Habituation on the Rotation-Nystagmus as Compared with the After-Nystagmus in the Rabbit, Am. J. Physiol. **68**:125-126 (March) 1924.

6. Griffith, C. R.: The Organic Effects of Repeated Bodily Rotation, J. Exper. Psychol. **3**:15-46 (Feb.) 1920.

7. Holsopple, J. Q.: Factors Affecting the Duration of Post-Rotation Nystagmus, J. Comp. Psychol. **3**:283-304 (Aug.) 1923.

8. Dunlap, K.: The Nystagmus Test and Practice, J. A. M. A. **73**:54-55 (July 5) 1919.

9. Dodge, R.: Habituation to Rotation, J. Exper. Psychol. **6**:1-35 (Feb.) 1923.

10. Mowrer, O. H.: (*a*) The Influence of "Excitement" on the Duration of Post-Rotational Nystagmus, Arch. Otolaryng. **19**:46-54 (Jan.) 1934; (*b*) An Analysis of the Effects of Repeated Bodily Rotation, with Especial Reference to the Possible Impairment of Static Equilibrium, Ann. Otol., Rhin. & Laryng. **43**:367-386 (June) 1934; (*c*) Some Neglected Factors Which Influence the Duration of Post-Rotational Nystagmus, Acta oto-laryng. **22**:1-23, 1935; (*d*) footnote 1; (*e*) "Maturation" vs. "Learning" in the Development of Vestibular and Optokinetic Nystagmus, J. Genet. Psychol. **48**:383-404 (June) 1936.

out if the rotation were to be prolonged at the same rate. Actually, this appears to be the case in a number of the individual tests made in our series. In these tests rotational nystagmus continued up to a certain number of turns and then ceased. In some instances the same end point in number of turns was reached in successive rotations at similar rates of turning. In these cases there was uniformly more postrotational nystagmus, often of comparable amounts in successive tests. However, if fixation was maintained in the animal, producing an optokinetic type of nystagmus in an attempt to maintain orientation in space, the rotational response persisted throughout the period of turning. The animal then showed a corresponding reduction in postrotational nystagmus. It is probable, then, that both the attempts at fixation occurring during rotation and the fixation following deceleration are responsible for reduction in postrotational responses.

That the optokinetic nystagmus present during rotation can carry over as an inhibitory influence on response following deceleration has been substantiated further by the results with animal 7 in our series. Here, in several instances, the quick and slow components of the optokinetic response failed to reverse after deceleration. Instead of the expected postrotational vestibular response, the same ocular movements persisted which had been observed during rotation. In all the instances (indicated by dagger) in which this occurred (see table) the response during rotation was continuous. This appears, then, to demonstrate that an optokinetic impulse can carry over into the postrotational period and correlates with the results of Mowrer.[10c] He found that pigeons which were rotated in the light and then placed in a darkened environment during the postrotational period showed this "inverse" postrotational effect. Attempts at fixation following rotation were eliminated by darkness; so the end effect must have been due to persistence of the optokinetic rotational stimulus.

Why such a response occurred in animal 7 of our series without the environment being darkened presents an interesting question. Mowrer's results in all his experiments with pigeons were surprisingly uniform. He also stated that the rabbit is not a suitable animal for such tests because of the variability of its responses. However, the basic structural differences between the avian and the mammalian brain may explain this apparent discrepancy. On the one hand, the pigeon, possessing a brain which has greatly enlarged basal ganglions and a relatively small amount of primitive cortex, has responses which are stereotyped. The mammalian subject, on the other hand, with the addition of a cerebral cortex, should present a variable response, conditioned by the level of cortical activity at the time of the experiment. Therefore variability should be the expected result, rather than stereotyped uniform response. This factor was well demonstrated by the

results gained on the seventh consecutive day of rotation. Here the animals, which were apparently lacking in attention because of the late evening hour during which the tests were performed, demonstrated a much greater postrotational response, and in 2 cases this was even greater than that seen at the start of the series. This would seem to indicate that a certain measure of cortical modification of the responses existed from the beginning and would also explain the individual variations between our animals recorded for the first day. It is obvious that there is danger in applying, unmodified, the results gained from experimentation on avian subjects to an analysis of the conclusions derived from experiments on man, since in the human brain the peak of cortical activity is reached.

The neuroanatomic background of the effects observed is not entirely clear. Mowrer [10] expressed the belief that the symptoms of nausea, vertigo, falling and past pointing seen with vestibular stimulation are likely due to stimuli resulting from the ocular motion produced by such vestibular activity. The point of origin of both the quick and the slow component of vestibular nystagmus has been shown to lie in the brain stem, the slow deviation being a direct result of action of the vestibular stimulus through the vestibular nuclei, and the quick return arising from the adjoining reticular substance (Lorento de Nó [11]). That the quick component of vestibular nystagmus is not cortical has been shown by Ivy.[12] Vestibular nystagmus, therefore, is thought to be a purely subcortical reflex phenomenon. Whether there is a cyclic repetition of stimuli in the vestibular nuclei occurring with the slow component, which then discharges the reticular impulse to produce the quick component, or whether the reticular substance discharges because of stimuli reaching it from a collicular level is not known. Ivy [13] expressed the opinion that the quick component of vestibular nystagmus was not produced by a cerebral reflex arc but was probably due to a reflex by way of the muscle centers of the eyes, which was excited by stimulation of the kinesthetic sensory nerve endings in the extraocular muscles.

In contrast to vestibular nystagmus, optokinetic nystagmus may follow cortical pathways, since the element of fixation is involved. The visual impulses which reach the calcarine fissure reflexly act through areas 18 and 19 of Brodmann, the visual psychic cortex, by way of the internal corticotectal tract to the nuclei of the cranial nerves which govern

11. Lorente de Nó, R.: Researches on Labyrinth Reflexes, Tr. Am. Otol. Soc. **22**:287-303, 1932.

12. Ivy, A. C.: Comparative Study of the Relation of the Cerebral Cortex to Vestibular Nystagmus, J. Comp. Neurol. **31**:1-16 (Oct.) 1919.

13. Ivy, A. C.: Physiology of Vestibular Nystagmus, Arch. Otolaryng. **9**:123-134 (Feb.) 1929.

movements of the eyes. Thus, fixation is maintained on the object, and a slow deviation results. Where the quick component of optokinetic nystagmus arises has not been demonstrated anatomically.

It is known that the quick return occurs in man when the deviation reaches a point beyond which head movement must occur in order to continue fixation. It is difficult to believe that the quick return can occur without the presence of proprioceptive stimuli from the extraocular muscles, although some investigators deny their existence. Adler [14] stated that "there is certainly no anatomic or physiologic proof that proprioceptive sensation is mediated from the ocular muscles." On the other hand, specialized sensory endings about the extraocular muscle fibers have been demonstrated by several workers. Maximow and Bloom [15] presented an illustration of such terminations. Hines [16] described specialized endings in the extraocular muscle fibers in the rabbit which were distinct from the motor end plates and which degenerated when the oculomotor nerve was sectioned at the base of the brain. Her work is well documented with photomicrographs. Woollard [17] observed similar endings in ocular muscle fibers and expressed the belief that his investigation suggested the origin of such nerve fibers to be in the mesencephalic nucleus of the trigeminal nerve, since degeneration was seen in this nucleus after section of the oculomotor nerve on the same side. The work of neuroanatomists on this problem has been well summarized by Ariëns Kappers, Huber and Crosby,[18] showing that the mesencephalic root of the trigeminal nerve may well be the site of cell bodies for such nerve endings. Corbin [19] suggested that the sensory fibers to the extrinsic ocular muscles may be largely unmyelinated and may arise from the small cell component of the mesencephalic nucleus at the level of the oculomotor nucleus, since he could not trace such fibers in Marchi preparations. Although no secondary pathway to the somesthetic cortex from these receptors is known, it still is evident that there is consciousness of the position of the eyes with the lids closed.

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14. Adler, F. H.: Pathologic Physiology of Convergent Strabismus: Motor Aspects of Nonaccommodational Type, Arch. Ophth. **33**:362-377 (May) 1945.

15. Maximow, A. A., and Bloom, W.: A Textbook of Histology, ed. 4, Philadelphia, W. B. Saunders Company, 1942, fig. 174.

16. Hines, M.: Studies on the Innervation of Skeletal Muscle: III. Innervation of the Extrinsic Eye Muscles of the Rabbit, Am. J. Anat. **47**:1-53 (Jan.) 1931.

17. Woollard, H. H.: The Innervation of the Ocular Muscles, J. Anat. **65**:215-223, 1931.

18. Ariëns Kappers, C. U.; Huber, G. C., and Crosby, E. C.: The Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company, 1936.

19. Corbin, K. B.: Observations on the Peripheral Distribution of Fibers Arising in the Mesencephalic Nucleus of the Fifth Cranial Nerve, J. Comp. Neurol. **73**:153-177 (Aug.) 1940.

If such an impulse reaches the higher centers, then the quick component may be produced by cortical motor centers.

The location of the mesencephalic nucleus is such that it might be possible for direct connections to exist in the midbrain between its fibers and the neurons constituting the nuclei of the extraocular muscles. In this way, the quick return movement may be produced. There is no work confirming or disproving this point, although cells of the mesencephalic nucleus lie in the midbrain, some of them very close to the oculomotor nucleus, or rarely in it. Others lie in the anterior medullary velum, close to the emerging roots of the trochlear nerve.[18]

Another possibility is that the reticular centers of the brain stem play a role in the mechanism underlying the quick component of optokinetic nystagmus similar to that which they play in producing the quick component of vestibular nystagmus. The superior colliculus and the underlying regions, or tegmentum of the midbrain, are known to give rise to fibers which pass downward to the reticular formation of the brain stem. Thus the discharge, whether it arises from cortex or from proprioceptive connections direct to the motor centers of the extraocular muscles, could be sent by way of tectoreticular pathways to the reticular substance at the level of the vestibular nuclei, producing the quick return. This raises the question whether the quick component of the vestibular nystagmus might not also be mediated by such connections.

In the phylogenetic development of extraocular reflex connections, it is known that submammalian forms, either lacking a cortex or having a less differentiated cortex than mammals, have a definite pattern of optic nerve fiber endings which is laid down on the superior colliculus. In these forms optokinetic nystagmus is probably subcortical in nature. As the cortex develops and a secondary connection of the optic nerve fibers into the calcarine region by way of the lateral geniculate nucleus appears, there are progressively fewer fibers which reach the superior colliculus. Optic nerve fibers are still present in mammals, including some primates; they turn off to the superior colliculus without terminating in the lateral geniculate nucleus. Such a pathway to the colliculus has been noted in rabbits and monkeys (Brouwer[20]). These connections are to be differentiated from the pupillomotor fibers of the optic nerve, which turn off to the pretectal nucleus before reaching the lateral geniculate nucleus. It is evident, then, that there is a gradual shift in the proportion of afferent ocular connections from collicular to cortical levels, with a corresponding development of the colliculus into an important discharge path from the visual psychic areas of the cortex.

20. Brouwer, B.: Anatomical, Phylogenetical and Clinical Studies on the Central Nervous System (Herter Lecture for 1926), Baltimore, Williams & Wilkins Company, 1927.

It seems altogether probable that with the anatomic shift there is a corresponding functional shift of optokinetic functions from the superior colliculus to the cortex.

There is, however, the possibility that some subcortical reflex responses are present in higher forms in reaction to visual stimuli, and that optokinetic nystagmus, for example, could still occur in the absence of the calcarine area. Scala and Spiegel [21] presented work done on the dog and the cat which suggests that optokinetic nystagmus can be subcortical. In carnivores it is generally recognized that there are relatively more of the optic nerve fibers given off to the superior colliculus than in primates. These authors also showed that lesions of the superior colliculus interfered with the "subcortical" optokinetic nystagmus, although they made no statement as to relative change of quick and slow components. It is true, moreover, that such lesions made in the superior colliculus region might well interfere with the corticotectal pathways reaching the extraocular muscles via the superior colliculus from the visual psychic cortex.

Whether such a finding would hold true for primates remains to be demonstrated. It is possible that the higher the form, the more the optokinetic nystagmus is cortical in nature and the less the effect of subcortical connections. This would correlate with observations relating to the "power of attention" of the subject in modifying vestibular effects through cortical activity.

Regardless of the final outcome of work in determining which connections are actually involved, it seems possible that proprioceptive impulses may govern the quick component of nystagmus, both vestibular and optokinetic. This problem requires further study, and future investigations are planned in an attempt to determine such a relationship.

A further comment on the variability of response noted by different workers seems to be indicated. As was stated earlier in this paper, it is probable that cortical factors play a large part in modification of response. Mowrer [1b] used the pigeon as an experimental subject, deriving stereotyped responses, which might be expected from an avian type of brain. The same author [1a] stated:

> . . . a variety of factors—presence or absence of vision, direction of rotation, emotional disturbance, relative duration of the successive rotation and rest intervals, fixation or non-fixation of the head, age and type of subject, etc.—may be influential in determining the rate and extent of nystagmus reduction produced by any given schedule of repeated bodily rotation.

Hoshino [2] noted a variability in responses of the rabbit on successive days. Ivy [12] reported a considerable variation in the individual rabbit

21. Scala, N. P., and Spiegel, E. A.: Mechanism of Optokinetic Nystagmus, Arch. Ophth. **21**:555-557 (March) 1939.

with the same stimulus and found that struggling inhibited the duration and number of movements of the "after-nystagmus." Mowrer [10a] presented evidence which "suggests that the duration of nystagmus is conditioned by a 'central' mechanism." He noted, further, that variations which are not vestibular could be explained by assuming that such a "central" mechanism might be modified by "characteristic differences in nervous disposition as well as by temporarily prevailing neural conditions." These factors appear to explain the variability of response recorded for our series of animals and confirm the observation that variability may well be expected in species in which cortical factors modify the lower reflex responses.

SUMMARY AND CONCLUSIONS

Vestibular postrotational nystagmus is capable of modification by optokinetic nystagmus. In most cases of our series postrotational response was abolished by repeated daily rotation. This suggests that cortical influences are dominant over those of the vestibular level.

There appears to be a poststimulus persistence of optokinetic rotational nystagmus which is effective in reducing postrotational response. Our findings tend to support those of Mowrer in this respect.

Variability of response has been shown to be the expected finding in the higher forms which possess a well differentiated cerebral cortex. This tends to render less valid work which has been done using lower species whose response is mainly reflex in type. This also supports the accumulating mass of evidence which invalidates the Bárány test as a precise diagnostic aid.

The neuroanatomic background of optokinetic nystagmus is discussed and further lines of research are suggested.

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CHANGES IN RETINAL ARTERIOLES ASSOCIATED WITH THE HYPERTENSIONS OF PREGNANCY

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DURING the past fourteen years I have studied the eyegrounds of approximately 2,500 women suffering from hypertension during pregnancy. In two previous reports [1] the observations made on some of these patients were analyzed and an attempt was made to correlate the changes in the eyegrounds with the degree of toxemia. It was found that the frequency and degree of such changes more closely followed the severity of hypertension, and consequently the toxemia, than any other single laboratory or clinical sign. The one outstanding and consistently reliable change observed in the eyegrounds was the degree of general and localized spastic constriction of the retinal arterioles.

ANATOMY OF THE RETINAL ARTERIOLES

Knowledge of the structure of the walls of the retinal arterioles helps one to understand better the local manifestations of angiospasm. The central artery in the optic nerve has the same histologic characteristics in microscopic sections as arteries of similar size in other parts of the body. Its muscular coat has a thickness of about one-eighth the diameter of the lumen of the artery. But, as Friedenwald [2] stated:

> On passing through the cribriform lamina the artery is very markedly altered. The internal elastic lamella becomes reduced to a single thin layer and disappears entirely after the first or second bifurcation. The muscular coat becomes reduced to a single layer of muscular fibers, and after one or two bifurcations the fibers no longer form a continuous layer but are separated from one another by small gaps. Since, by definition, arteries which do not possess an internal elastic lamella nor a continuous muscular coat are classified as arterioles, the whole retinal arterial tree except for those branches in or close to the optic disc is arteriolar.

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This paper was accepted as the candidate's thesis in partial fulfilment of the requirements for membership in the American Ophthalmological Society by the Committee on Theses.

1. Hallum, A. V.: (*a*) Eye Changes in Hypertensive Toxemia of Pregnancy: Study of Three Hundred Cases, J. A. M. A. **106**:1649 (May 9) 1936; (*b*) Eye Changes in Management of Hypertensive Toxemia of Pregnancy: Five Year Study, South. M. J. **31**:64 (Jan.) 1938.

2. Friedenwald, J. S., in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, New York, Paul B. Hoeber, Inc., 1940, p. 77.

ESSENTIALS OF OBSTETRIC OPHTHALMOSCOPY

The present discussion is intended primarily for the obstetrician, appealing to him to do his own ophthalmoscopy. Of course, the best time to learn to use the ophthalmoscope is during the internship, when one is younger and more adept at learning new procedures. However, the obstetrician who had no training in the use of the ophthalmoscope during his hospital days can within a few weeks acquire the ability to gain invaluable information from the eyegrounds of almost every patient exhibiting hypertension during pregnancy. During the course of severe and moderately severe toxemia of pregnancy the most information is gained from the eyegrounds by making repeated examinations daily or every few days. A consultant ophthalmologist will be called in only once, or not at all; and if the obstetrician cannot do his own ophthalmoscopy the patient is the loser. Occasionally, she pays with her life or with the life of her baby when the obstetrician does not recognize the progress and severity of the toxemia and fails to terminate pregnancy. The eyegrounds are probably the best single indicator of the progress and severity of the toxemia.

In the early stages of learning the use of the ophthalmoscope, some help in the fundamentals from one's fellow ophthalmologist will be of great value. A good ophthalmoscope is essential, preferably one with the May head, and the illumination must always be bright. The most satisfactory ophthalmoscope and source of light is the giant electric ophthalmoscope, which operates off the house current, and the same small portable transformer is used as that which operates the usual office cautery.

Another essential requirement for good ophthalmoscopy is the dilation of the pupils. With instillation of 1 drop of a weak mydriatic, such as paredrine hydrobromide ophthalmic,[3] the pupils will be semidilated in twenty or thirty minutes. They will remain semidilated for an hour or two, but accommodation is only slightly impaired. The examination of the fundi can be much more efficiently done in a semidark or dark room. If the patient is to go out into bright sunshine after this examination, it might be preferable to hasten the contraction of the pupils by instilling into each eye 1 drop of a weak miotic, such as 0.1 per cent physostigmine salicylate or 0.5 per cent pilocarpine nitrate. However, the patient should be warned that in a few minutes she will probably experience twitching of her lids, and possibly a drawing sensation in her eyes. This ciliary spasm lasts only a few minutes but often produces much more discomfort than does the small amount of photophobia, and for that reason the miotic had probably best be omitted.

3. Paredrine hydrobromide ophthalmic is a 1 per cent solution of p-hydroxy-α-methylphenylethylamine hydrobromide in distilled water, made tear isotonic with 2 per cent boric acid and preserved with merthiolate, 1 : 50,000.

The possibility of acute glaucoma being produced by the dilation of the pupils is remote, since glaucoma is rare in women of the child-bearing age. However, if acute glaucoma should be precipitated, the patient will complain of more or less severe pain in or about the eyes, and her vision will be noticeably impaired by the haziness of the corneas. The eyeballs will feel hard when palpated through the upper lids, and the pupils will be dilated. If acute glaucoma should be suspected, a miotic should be instilled into each eye six times at intervals of fifteen minutes, and the patient referred to an ophthalmologist. I have seen acute glaucoma develop in only 1 patient after this routine mydriasis, and it was considered that she was fortunate in having her glaucoma discovered before it produced loss of vision.

SPASMS OF RETINAL ARTERIOLES

The first change observed in the normal retinal arterioles during a true toxemia of pregnancy is constriction of the lumen. In some patients this constriction may be localized to a single point, resembling a sausage-link constriction, as though a single fine silk thread partially constricted the arteriole. There can be a series of these localized constrictions, some elongated and spindle shaped and usually limited to the first half of the retinal arteriole. This is the portion of the arteriole nearest the optic disk, and the constrictions are seen more frequently in the nasal branches. These elongated, spindle-shaped constrictions appear as uniformly symmetric indentations of both sides of the arteriole and resemble the constriction that would be produced by stretching a glass tube, the middle section of which had been heated almost to the melting point. In searching for these localized constrictions, the examiner must adjust the ophthalmoscope to its very best focus, and if while looking at a section of an arteriole he slowly rotates the ophthalmoscope to and fro he will often bring the outline of the constrictions into better view.

In other patients the first change observed may be a generalized arteriolar constriction, so that, instead of the diameter ratio of vein to arteriole being the normal 3:2, the arterioles may be constricted so that the ratio is 2:1. As the severity of the toxemia progresses, the arterioles are usually seen to become more constricted, until the ratio increases to 3:1 or more. Usually the patients showing generalized arteriolar constriction also exhibit varying degrees of localized constriction. When there is a generalized arteriolar constriction beyond the ratio of 2:1, it is increasingly difficult to recognize localized variations in the diameter of the lumen. The addition of a localized spastic condition indicates an active progressive toxemia.

In estimating the vein-arteriole ratio, the examiner must be sure that he is comparing the diameter of a principal vein and its corresponding arteriole. The best place to make this determination is about

1 disk diameter from the margin of the disk, using either the superior or the inferior temporal vessels and being sure that neither the vein nor the arteriole has divided before reaching that point. If either the vein or the arteriole has divided before reaching the point of comparison, a wrong ratio will be obtained.

The arteriolar constrictions are proved to be spastic in nature when the degree and location can be seen to vary at subsequent examinations. Many patients were examined a few days after delivery, when the blood pressure had returned to normal and the formerly constricted arterioles had resumed their normal caliber and normal ratio. These constricted arterioles did not show compression of the veins at the

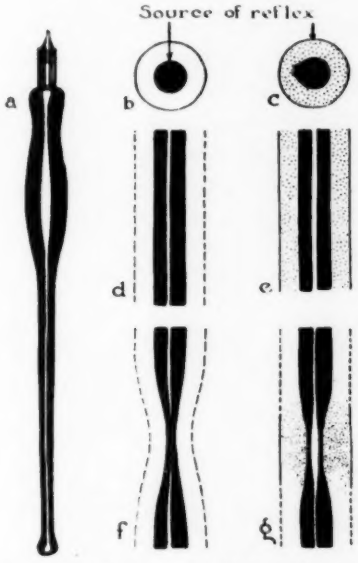

Fig. 1 (from Gans [4]).—Variations in the light reflex (see text for details).

arteriovenous crossing, nor did they show increased light reflex stripe. In fact, when there is noticeable angiospasm, the light reflex is actually decreased.

Gans [4] recently explained in a simple and convincing manner why the light reflex is actually narrower in angiospasm and, at the same time, why it is wider in sclerosis. He cited Duke-Elder,[5] who pointed out that in the normal fundus one sees the blood column only, and not the vessel, the wall of which is transparent. Gans cited Wilmer, Pierce

4. Gans, J. A.: Classification of Arteriosclerotic-Hypersensitive Fundus Oculi in Patients Treated with Sympathectomy, Arch. Ophth. **32**:267 (Oct.) 1944.

5. Duke-Elder, W. S.: Text-Book of Ophthalmology, London, Henry Kimpton, 1940, vol. 3, p. 2677.

and Friedenwald,[6] who stated that the reflex stripe is produced by the reflection of light from the surface of the blood column and from the surface of the vessel wall. In normal arterioles the main source of reflected light is the surface of the blood column, as illustrated in figure 1*b* and *d*. He compared the light reflex of the normal arteriole to the light reflx from the surface of a penholder, showing that the light reflex is proportional to the diameter of the reflecting surface, as illustrated in figure 1*a*. When the arteriolar wall has undergone sclerosing changes, it is made optically denser, and its surface reflects proportionately more light, as illustrated in figure 1*c* and *e*.

A spasm seen in a normal arteriole is illustrated in figure 1*f*. Since the surface of the blood column is narrowed by the constriction of the arteriolar wall, the light reflex is also narrowed. Figure 1*g* represents a sclerosed arteriole the blood column of which has been narrowed by thickening of the vessel wall and intimal proliferation. Actually, in sclerosis the constriction is usually unsymmetric. The widened reflex at the site of narrowing of the blood column indicates that the thickened wall is producing most of the reflex and that the thickening of the arteriolar wall is greatest in this section.

CLASSIFICATION OF RETINAL ARTERIOLAR SPASM

For the convenience of description, the following classification of retinal arteriolar spasm in toxemia of pregnancy is suggested. The classification is based on the degree of arteriolar spasm and usually indicates the severity and duration of the toxemia.

GRADE 1.—The spasms are localized and may be limited to one or more points. They are usually seen in the proximal portion of the arterioles. The general diameter ratio of vein to arteriole is the normal ratio of 3 : 2, or there may be a slight increase in this ratio.

GRADE 2.—The arterioles show a generalized constriction so that the diameter ratio of vein to arteriole is 2 : 1. Usually there are also localized constrictions of the arterioles.

GRADE 3.—The degree of generalized arteriolar constriction has increased until the diameter ratio of vein to arteriole is 3 : 1. Fine localized constrictions in the arterioles are usually present but are difficult to distinguish.

GRADE 4.—The degree of generalized arteriolar constriction has progressed until the diameter ratio of vein to arteriole is 3 : 1 or more, and there is some degree of retinopathy. (Retinopathy will occasionally be seen in arteriolar spasm of grade 3, or even of grade 2, especially

6. Wilmer, W. H.; Pierce, H. F., and Friedenwald, J. S.: Light Streaks on Retinal Blood Vessels, Arch. Ophth. **9**:368 (March) 1933.

if the localized constrictions are pronounced and the toxemia is sudden and severe.)

ARTERIOLAR SPASMS SUPERIMPOSED ON ARTERIOLAR SCLEROSIS

Spastic arteriolar constrictions are often seen superimposed on chronic vascular disease, indicating that the existing toxemia of pregnancy has caused spastic constrictions of arterioles that previously had

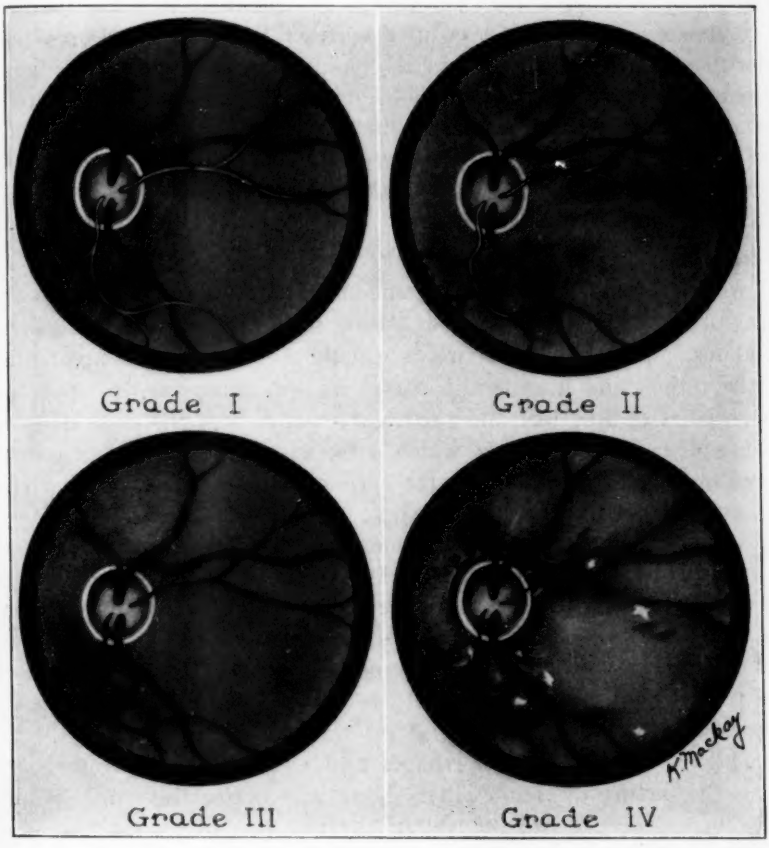

Fig. 2 (Hallum).—Drawings illustrating classification of retinal arteriolar spasm (see text for details).

undergone sclerotic changes. When branches or portions of branches of the arterioles show constriction without an increase (or indeed with a decrease) in the light reflex it is likely that angiospasm is present.

Sclerotic changes are indicated by the usual signs of retinal arteriolar sclerosis, the most reliable being that of compression of the vein at the arteriovenous crossing. Unsymmetric constrictions of the lumen of the

arterioles, in contrast to the symmetric constrictions seen in angiospasm, are an indication of organic change in the arteriolar wall. The reflex stripe is an unreliable guide in estimating retinal arteriolar sclerosis, but when there is a marked increase in the light reflex stripe or when narrowed portions of an arteriole show an increase in the light reflex it is likely that there is vascular disease. Increased tortuosity of the arterioles is usually not seen until an advanced degree of arteriolar sclerosis has occurred, and then it is best seen in the terminal and very small arterioles. In a high percentage of such cases it is impossible on a single examination to be positive whether the changes are spastic or sclerotic in nature, or whether a combination of the two changes is present. If subsequent examinations, days, weeks or months later, reveal the disappearance of the arteriolar constrictions, it would be proof of their spastic nature; if the constrictions remain unchanged, or tend to increase, it would indicate permanent changes in the walls of the arterioles.

RETINOPATHY

As the retinal arterioles become more constricted, there are seen signs of retinal ischemia, such as edema of the retina, hemorrhages and exudates. Edema of the retina is usually the first sign of involvement of the retina, and it generally makes its appearance at the upper and lower poles of the disk and progresses away from the disk along the course of the retinal vessels, which is likewise the general course of the nerve fibers of the retina. In the earliest stage of edema of the retina the portion involved appears milky; and on close examination with the very best focus of the ophthalmoscope, and with a gentle and slow to and fro rotation of the hand holding the ophthalmoscope, the surface shows faint striations running in the direction of the nerve fiber layers. As the edema becomes more marked, the retina becomes fluffy, grayish and semiopaque and tends to cover or surround the retinal vessels. In the presence of retinal edema it is difficult to judge the degree of arteriolar constriction.

The appearance of hemorrhages and exudates in the retina completes the picture of retinopathy. Some still prefer the name retinitis, and others prefer to call the condition retinosis. The hemorrhages are usually in the posterior one third of the fundus, and as a rule appear flame shaped, indicating that they are in the superficial nerve fiber layer. The exudates have a similar distribution and vary in size from that of a pinhead to half the area of the disk.

The recently formed superficial exudates, that is, the exudates in front of the retinal vessels, are whitish and fluffy and have hazy margins. After these exudates have been present for a few days, they become glistening white and the margins become more distinct. The exudates which form in the deeper layers of the retina, and possibly in the choroid, appear as indistinct grayish clouds. These changes in the retina usually

disappear completely after the termination of the toxemia and subsequent improvement in the blood supply to the retina.

The earlier in pregnancy these toxic signs develop in the eyegrounds, the more serious is the prognosis. If retinopathy appears before the twenty-eighth week, there is only about a 25 per cent chance of the patient's giving birth to a live baby, even if the pregnancy is permitted to continue to the stage of viability. Wagener [7] reported similar findings and cited similar observations of Schiøtz [8] and Masters.[9]

DETACHMENT OF THE RETINA

In an occasional patient detachment of the retina will develop during severe toxemia of pregnancy. The detachment is usually bilateral and may or may not be accompanied with diffuse retinopathy. The detachment will usually become reattached spontaneously within ten to fourteen days after delivery. The portion of the retina that is detached is blind, but Benedict [10] pointed out that as soon as it comes in contact again with the choroid it begins to "see." Eight or ten years ago, I thought that retinal detachment occurred in approximately 2 per cent of cases of hypertensive toxemia of pregnancy, but now I am convinced that this complication occurs much less frequently. Schiøtz [8] found 7 instances of detachment among 158 cases of eclampsia and threatened eclampsia. Detachment of the retina complicating toxemia of pregnancy has been reported by many other observers.[11]

FREQUENCY OF CHANGES IN THE EYEGROUNDS

In 1936 from a study of 16 of 300 consecutive patients with hypertension during pregnancy, it was found that the eyegrounds showed changes produced by the hypertension in 76 per cent. As shown in the

7. Wagener, H. P.: Arterioles of Retina in Toxemia of Pregnancy, J. A. M. A. **101**:1380 (Oct. 28) 1933; Lesions of Optic Nerve and Retina in Pregnancy, ibid. **103**:1910 (Dec. 22) 1934.

8. Schiøtz, H.: Klin. Monatsbl. f. Augenh. **67**:1, 1921.

9. Masters, R. J.: Routine Ophthalmoscopic Examination as Aid in Management of Maternity Cases, Tr. Am. Ophth. Soc. **31**:416, 1933.

10. Benedict, W. L., in discussion on Kronfeld.[11g]

11. (*a*) Blake, E. M.: Bilateral Detachment of Retina in Nephritis of Pregnancy, Arch. Ophth. **51**:586 (Nov.) 1922. (*b*) Hill, E.: Bilateral Detachment of Retina in Two Successive Pregnancies, ibid. **53**:137 (March) 1924. (*c*) Richardson, S.: Case Report: Bilateral Retinal Detachment Complicating Toxemia of Pregnancy, J. Florida M. A. **16**:266 (Dec.) 1929. (*d*) Black, N. M.: Ocular Disturbance in Pregnancy and During Puerperium, ibid. **18**:121 (Sept.) 1931. (*e*) Crowther, W. L., and Hamilton, J. B.: Eclampsia with Amaurosis Due to Detachment of Retinæ, M. J. Australia **2**:177 (Aug. 6) 1932. (*f*) Wagener.[7] (*g*) Kronfeld, P. C.: Function of Reattached Retina, Arch. Ophth. **10**:646 (Nov.) 1933. (*h*) Jaffee, M.: Retinal Detachment in Toxemias of Pregnancy: Report of a Case, ibid. **10**:454 (Dec.) 1933.

table, an increase in the frequency of the changes in the eyegrounds became apparent with an increase in the severity and duration of the hypertension. Class I includes the patients whose blood pressure before delivery was below 150 systolic and 100 diastolic; in class II are placed those patients whose blood pressure varied from 150 systolic and 100 diastolic to 175 systolic and 125 diastolic, and class III consists of the patients whose blood pressure was 175 systolic and 125 diastolic or more. Thus, it is seen that changes in the eyegrounds were found in 41 per cent of the patients in class I, in 84 per cent of the patients in class II and in 98 per cent of the patients in class III. Since these surveys were made, my colleagues and I have learned to give more attention to the presence of

Relation of Positive Signs, Expressed as Percentages, and of Other Data to Severity of the Hypertension in a Series of Three Hundred Women with Hypertension During Pregnancy *

	Classes of Hypertension		
	I	II	III
Changes in eyegrounds	41.0	84.0	98.0
Retinopathy	3.7	9.9	32.7
Albuminuria	46.0	63.0	68.0
4 plus albuminuria	3.3	9.2	26.0
Casts in urine	7.6	20.0	26.0
Low output of phenolsulfonphthalein	43.8	41.8	45.2
Retention of nonprotein nitrogen	....	....	5.6
Abnormal gain in weight (last trimester, 40 cases)	....	....	7.5
First pregnancy	42.4	38.7	20.0
Sixth (or more) pregnancy	15.1	21.7	52.0
Average age	23.0	24.9	30.2
Labor induced	15.2	36.7	60.0

* After Hallum.[1b]

arteriolar constriction and to recognize even a single localized constriction. Now changes are found in the eyegrounds of approximately 100 per cent of the women who have pressures as high as 150 systolic and 90 diastolic for two or three days or longer.

Among other data, the table shows that albuminuria is often absent even in cases of severe toxemia and that the phenolsulfonphthalein excretion test is of no value with this condition. But it will be noted that the frequency of 4 plus albuminuria, casts in the urine and retinopathy is in proportion to the severity of the hypertension.

DIFFERENTIATION OF TYPES OF TOXEMIA

Interpretation of the changes in the eyegrounds often aids in differentiating the type of toxemia present. In preeclampsia and eclampsia the outstanding change is spastic localized and generalized constriction of the arterioles, and the degree of constriction usually is found to be

in proportion to the severity of the toxemia. When the angiospasm is severe, retinopathy appears.

Such spastic changes are found most often in the last trimester of pregnancy and are much more common in primiparas, especially young primiparas. This is because true toxemia occurs much more frequently in young women, especially during the first pregnancy. If the angiospasm did not exist long enough to cause organic changes in the walls of the arterioles throughout the body, the blood pressure returns to normal within a few days after delivery and remains so permanently, and the retinal arterioles soon resume their normal caliber. An increase in the uric acid content of the blood above 3.5 mg. per hundred cubic centimeters tends to indicate that the hypertension is of toxic origin, and peripheral resistance is actually produced by spasm of the arterioles. When the uric acid content of the blood is normal in a toxic patient who shows constriction of her retinal arterioles it is likely that vascular disease is the basis of the toxemia.

If the eyegrounds show only the signs characteristic of retinal arteriolar sclerosis, such as arteriovenous compression, unsymmetric arteriolar constrictions and increased light reflex, the hypertension is explained by vascular disease which antedated the present pregnancy. Vascular disease accounts for most cases of hypertension during the first two trimesters of pregnancy, and unless the hypertension is severe there are usually no toxic symptoms or positive laboratory findings. However, the hypertension of chronic vascular disease usually becomes accentuated during pregnancy.

Occasionally, angiospasm is superimposed on an eyeground showing changes characteristic of chronic vascular disease, indicating that preeclamptic toxemia is superimposed on chronic vascular disease. Such an ocular fundus will show arteriolar constrictions, localized and generalized, out of proportion to the evidence of vascular disease. It is usually impossible on a single examination to be positive of such a combination of changes, but if subsequent examinations reveal a decrease in the arteriolar constriction it is proof of the presence of angiospasm.

As emphasized by McCord [12] and Stander,[13] the greatest factor in differentiating the various hypertensions of pregnancy is a long period of observation. The past history must be considered, together with repeated checks on the blood pressure, study of the eyegrounds, urinalysis, renal function tests, determinations of the uric acid content of

12. McCord, J. R.: Premature Rupture of Membranes as Method of Inducing Labor, Am. J. Obst. & Gynec. **38**:587 (Oct.) 1939.

13. Stander, H. J., in Williams, J. W.: Obstetrics: Textbook for Use of Students and Practitioners, ed. 8, New York, D. Appleton-Century Company, Inc., 1941, p. 645.

the blood, etc. McCord [12] gave Bartholomew credit for the following observation:

> A practical point that will often help in the differentiation of preeclampsia and chronic vascular disease is that bed rest, as a rule does not lower the blood pressure in preeclampsia but does lower the blood pressure in chronic vascular disease.

I am not sure that I have ever seen an eyeground that indicated acute nephritis (acute glomerulonephritis) complicating pregnancy. This type of renal disease has a sudden onset and is characterized by marked edema, albuminuria, decreased renal function and subsequent hypertension. In acute nephritis of pregnancy one would expect to find the same changes in the eyegrounds that are found in acute nephritis from other causes, namely, retinopathy, and in the early stages there would be an absence, or only a slight degree, of spasm of the arterioles. If the condition persists for several days or weeks, there will be seen to develop an increasing degree of angiospasm. Preexisting renal disease manifests itself in the eyegrounds only by the degree of generalized vascular disease that resulted from the previous nephritis.

Many patients with postpartum eclampsia have been examined, and most of them showed normal eyegrounds the first day or two after the sudden appearance of the severe toxemia. However, if the hypertension persists, within a few days there appear localized and generalized arteriolar constrictions, which tend to disappear as the hypertension subsides.

In March 1944, a questionnaire was mailed to the chiefs of the departments of obstetrics of the seventy-four grade A medical schools of the United States and Canada. The purpose of the questionnaire was to determine the frequency, and to learn the opinions concerning the relative value, of the study of the fundus oculi in the management of hypertension during pregnancy. Some of the facts learned from sixty-nine questionnaires which were answered follow:

1. Eighty-five per cent of the department chiefs feel that the information gained from the study of the eyegrounds helps in the management of hypertension during pregnancy.

2. Seventy-five per cent of the department staffs routinely study the eyegrounds of patients with hypertension during pregnancy.

3. Fifty per cent of the chiefs whose department staffs routinely study the eyegrounds of patients with hypertension during pregnancy rank the value of this information as of equal importance or as second in importance to the value of blood pressure determinations.

4. Forty per cent of the department staffs require the house officers, as part of their training, to study the eyegrounds of patients with hypertension during pregnancy.

Dr. Henry P. Wagener, of the Mayo Clinic, suggested that I check the findings of Suganuma,[14] who compared the pressure in the brachial artery with that in the central retinal artery in patients with hypertensive toxemia of pregnancy. He made these determinations from one to four times on 10 patients, making a total of 20 determinations on the 10 patients. He listed several positive conclusions on the basis of his study of these 10 patients, and probably his most striking conclusion was that "in toxemia appearing in healthy primiparas an increase in retinal arterial pressure is the first appearing and probably the only inevitable sign of preeclampsia." When the retinal and brachial systolic and diastolic blood pressure readings in his cases are recorded graphically on the same chart, it is seen that there is a uniform tendency for the retinal arterial pressure to vary in proportion to the brachial arterial pressure.

Dr. Wagener loaned me his Bailliart ophthalmodynamometer, and I compared the brachial and retinal arterial pressures in 50 consecutive cases of toxemia of pregnancy. When my readings were recorded graphically on the same chart, they were, in general, similar to those of Suganuma; that is, the retinal systolic and diastolic pressures usually showed a general pattern in conformity with the brachial systolic and diastolic pressure. I was unable to find any consistent variations in the relationship of these graphs that might be characteristic of the severity or the type of toxemia. In general, I agree with Koch [15] that individual ophthalmodynamometric readings alone are of no real clinical value in classifying patients with hypertension because the pressure in the central retinal artery varies too much in proportion to the pressure in the brachial artery.

REVIEW OF THE LITERATURE

Only four years after the invention of the ophthalmoscope by von Helmholtz, von Graefe,[16] in 1855, first described the retinopathy of pregnancy. Silex,[17] in 1895, reported the first large series, of 35 cases, and he expressed the belief that retinopathy occurred once in about 3,000 pregnancies. Miller [18] found 6 patients with retinopathy in 1,800 pregnancies.

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14. Suganuma, S.: Studien über den Blutdruck in der Zentralarterie der Netzhaut; über den Blutdruck in der Netzhautarterie während des Verlaufes der normalen Schwangerschaft und der Schwangerschaftstoxikose, sowie über seine frühdiagnostische Bedeutung, Klin. Monatsbl. f. Augenh. **99**:637 (Nov.) 1937.

15. Koch, F. L. P.: Retina in Systemic Vascular Hypertension: Clinical Study of Caliber of Retinal Arterioles and Retinal Arterial Diastolic Blood Pressure, Arch. Ophth. **26**:565 (Oct.) 1941.

16. von Graefe, F. W. E., cited by Cheney.[20]

17. Silex, P., cited by Cheney.[20]

(Footnotes continued on next page)

Woods [19] and Miller seem to have expressed the prevailing opinion up to about 1915 concerning the significance of retinopathy. Woods asserted that toxemia of pregnancy was the result of an unknown substance circulating in the blood and that this toxic substance was responsible for the changes observed in the eye, kidney and liver. He recognized that this substance produces thrombosis in many smaller vessels, with resulting degenerative changes in various parts of the body. Retinopathy, in his opinion, was an indication for promptly emptying the uterus, even in the absence of albuminuria.

Miller was the first obstetrician to attempt to correlate changes in the eyegrounds with the toxemia of pregnancy. He did his own ophthalmoscopy but had an ophthalmologist corroborate his findings in most cases. The outstanding point he stressed was that retinal lesions are found only with nephritic toxemia and that when nephritis is present in toxemia of pregnancy the renal lesion is primary and more or less extensive. In his opinion, retinopathy was not only an indication for immediate termination of the pregnancy but was also an indication for sterilization to prevent future pregnancies. Neither Woods nor Miller mentioned the status of the retinal arterioles.

In 1924, before the Section on Ophthalmology of the American Medical Association, Cheney [20] reviewed the literature and in a masterful manner correlated the obstetric and ophthalmologic point of view. His observations and conclusions were based largely on the newer concept of the cause of toxemia of pregnancy, namely, the contraction of the capillary and precapillary vessels, including those of the kidney. Volhard,[21] according to Cheney, was among the first to state that retinopathy, and similar changes in other organs of the body, resulted from ischemia. Volhard claimed that the changes seen in the glomeruli in cases of nephritis were not a manifestation of an inflammatory process, but were simply an ischemic or asphyxial change secondary to a diminution of the blood supply. He found constricted arterioles in every case of retinopathy, and histologically the same vascular changes were observed in the renal vessels. Cheney cited Hewlett,[22] who concluded that the action of a toxic substance caused the systemic arterioles to con-

18. Miller, J. R.: Relation of Albuminuric Retinitis to the Toxemias of Pregnancy, Am. J. Obst. & Gynec. **72**:253, 1915.

19. Woods, H.: Ocular Complications of Pregnancy, J. A. M. A. **51**:204 (July 18) 1908.

20. Cheney, R. C.: Toxemias of Pregnancy from Ophthalmologic Standpoint, J. A. M. A. **83**:1383 (Nov. 1) 1924.

21. Volhard, J.: Ber. ü. d. Versamml. d. ophth. Gesellsch., 1916.

22. Hewlett, A. W.: Pathological Physiology of Internal Diseases, New York, D. Appleton and Company, 1917.

strict and thus produce hypertension. Silex, in 1895, mentioned narrowing of the retinal arterioles.

In a large number of toxemic patients at the Boston Lying-in Hospital, Cheney found narrowing of the retinal arterioles in most of those who had marked hypertension, and the constriction was dependent only on the hypertension, and not on whether the condition was acute toxemia or nephritis. He reasoned that in toxemia of pregnancy the vasoconstriction is sudden and retinopathy often develops because the retina does not have time to "compensate," or adjust to the diminished blood supply, whereas in arteriolar sclerosis of long standing the constriction of the arterioles is often more pronounced but the frequency of retinopathy is much less because the change is slow in developing and the retina has time to compensate. He expressed the belief that in the majority of cases one cannot differentiate between the acute toxemia and chronic nephritis by the fundus picture alone, because often the preexisting chronic nephritis was not severe enough to cause vascular changes visible with the ophthalmoscope but did produce sufficiently extensive changes to cause a flare-up of the nephritis from the extra burden of pregnancy. In his opinion, in such cases there is retinal angiospasm similar to the acute toxemia. In the discussion of this paper, Drs. Allen Greenwood, William C. Posey, Edward Jackson and Arnold Knapp expressed agreement in general with the conclusions.

It is generally considered that angiospasms can exist for several days at least without becoming fixed or sclerotic. Keith [23] stated the opinion that spasms might occur and leave no demonstrable injury, as illustrated by the angiospasm present in eclampsia, which is relieved by the termination of pregnancy; on the other hand, if the spasms persist, organic changes occur in the vascular walls and the kidney. He stated that angiospasm is capable of producing anemic infarcts. According to Freeman, Mylius [24] demonstrated by a series of fundus photographs that angiospasm is an indisputable fact. Bergmann cited the histologic examinations by Mylius [25] of the eyes of patients who had died in eclampsia and concluded that functional constrictions can exist for many weeks without becoming sclerotic.

Disturbance of vision during the acute stage of the toxemia is frequent. In approximately half the 47 cases of late toxemia reported by Schultz and O'Brien [26] visual disturbances were complained of. My

23. Keith, N. M.: Tr. Am. Acad. Ophth. **30**:37, 1932.

24. Mylius, K., cited by Freeman, D.: Am. J. Ophth. **16**:341, 1933.

25. Mylius, K., cited by Bergmann, M. B.: Relationships Between Ophthalmology and Obstetrics, Am. J. Ophth. **17**:141 (Feb.) 1934.

26. Schultz, J. F., and O'Brien, C. S.: Retinal Changes in Hypertensive Toxemia of Pregnancy: Report of Forty-Seven Cases, Am. J. Ophth. **21**:767 (July) 1938.

observation has been that vision is noticeably impaired when the retina in the macular region is edematous or when the macula is covered with hemorrhages or exudates. Vision in these situations is usually restored to normal or near normal when the toxic state is relieved. However, when detachment of the retina involves the macular region, the vision is seriously impaired at that time; and even after the retina is reattached the central visual acuity remains permanently impaired, often by as much as 50 per cent.

Masters,[27] in 1933, reported his findings in the routine ophthalmoscopic examination of 269 patients, beginning in many instances with the early prenatal visits. In 15.2 per cent of these patients slight retinal venous dilatation was present during the early months of pregnancy but disappeared by the eighth or ninth month. He found a generalized uniform constriction of the retinal arterioles in all patients whose systolic blood pressure was elevated to 150 mm. of mercury. In 32 patients with severe toxemia, 10 out of 17 who had preexisting nephritis lost their babies, while only 4 out of 15 who did not have preexisting nephritis lost their babies. In his opinion, retinopathy is an urgent indication for termination of pregnancy, and mothers with retinal lesions in most instances will show permanent vascular and renal damage.

Wagener found spastic constriction of the retinal arterioles in about 70 per cent of women with hypertensive toxemia of pregnancy and considered it to be usually the primary sign of retinal involvement. In about 60 per cent of the patients the spastic lesions disappeared when pregnancy was terminated and the blood pressure returned to normal. In about 40 per cent of his patients organic lesions developed in the arterioles, and elevated blood pressure usually persisted. He did not consider retinopathy evidence of nephritis; instead, he stated that it indicated generalized arteriolar sclerosis. He showed by biopsy and at necropsy that the arterioles throughout the body were permanently damaged in patients with retinopathy and expressed the belief that the majority of them would have persistent hypertension.

Mussey[28] found that there was a definite increase in degree and severity of changes in the eyegrounds which was in proportion to the height and duration of the blood pressure. He asserted that the information gained from retinal examination is often a distinct aid in determining whether and when pregnancy should be terminated. He stated that examination of the eyegrounds early in pregnancy was of value in determining the presence of vascular disease, on which process might be seen the development of spastic lesions later in pregnancy.

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27. Masters, R. J.: Routine Ophthalmoscopic Examination as Aid in Management of Ninety-Three Maternity Cases, Tr. Am. Ophth. Soc. **31**:416, 1933.

28. Mussey, R. D.: Relation of Retinal Changes to Severity of Acute Toxic Hypertensive Syndrome of Pregnancy, Am. J. Obst. & Gynec. **31**:938 (June) 1936.

Gibson [29] reported 39 cases of hypertensive toxemia of pregnancy; in 5 the eyegrounds were normal, in 20 they showed preorganic arteriolar constriction and in 11 they showed organic changes. He agreed essentially with my general conclusion, but I disagree with him on two points of observation.

1. He stated that in spastic arteriolar constriction there is an accentuation of the light reflex. According to my observation, the light reflex in this condition is not increased but has a tendency to be actually decreased. This is an important point in the differentiation of constriction produced by spasm from the constriction produced by sclerosis.

2. He further stated that localized constrictions usually are seen first in the extreme periphery of the retinal arterioles and that as the constriction increases the process involves the vessels closer and closer to the optic disk. My findings have been just the opposite; the localized constrictions usually first involve the proximal one third of the retinal arteriole and progressively spread toward the periphery of the arteriole. However, Duke-Elder [30] and Lillie,[31] in their respective textbooks, have cited Gibson on these points.

According to Mussey and Mundell,[32] the section on Obstetrics at the Mayo Clinic since 1921 has been using the changes in the eyegrounds, as a guide in the management of toxemia of pregnancy. The findings on retinal examination were a distinct guide to the management of approximately 28 per cent of the patients during the first five years of this period, of 51 per cent in the second five years and of 56 per cent in the last five years. They state:

> The presence and degree of spasm of the retinal arteries has paralleled so closely clinical evidence of the severity of toxemia that we have increasingly depended on this examination.

Bartholomew and Colvin [33] presented the second study on hypertensive toxemia of pregnancy, based largely on the retinal examination, in which the ophthalmoscopic studies were done by the obstetrician. Miller reported the first study in 1915. Bartholomew and Colvin studied the eyegrounds of 286 consecutive patients throughout pregnancy and found that about one sixth showed slight to moderate arteriolar constric-

29. Gibson, G. G.: Clinical Significance of Retinal Changes in Hypertensive Toxemias of Pregnancy, Am. J. Ophth. **21**:22 (Jan.) 1938.

30. Duke-Elder,[5] p. 2724.

31. Smith, L. W., and others: Cardiovascular Renal Disease, New York, D. Appleton-Century Company, Inc., 1940, p. 14.

32. Mussey, R. D., and Mundell, B. J.: Retinal Examinations: Guide in Management of Toxic Hypertensive Syndrome of Pregnancy, Am. J. Obst. & Gynec. **37**:30 (Jan.) 1939.

33. Bartholomew, R. A., and Colvin, E. D.: Interpretation of Blood Pressure Behavior During Pregnancy and Puerperium, Am. J. Obst. & Gynec. **42**:646 (Oct.) 1941.

tion early in pregnancy, even though the blood pressure was normal. Two thirds of the patients showing early arteriolar constriction had hypertension during the last four to six weeks of pregnancy. About nine tenths of the latter group apparently had vascular disease, and none had severe toxemia. Only one fourth of the patients who showed normal arterioles during early pregnancy had hypertension during the last four to six weeks of pregnancy. True toxemia during the last trimester developed three times as frequently in the group showing normal arterioles during early pregnancy as it did in the group showing arteriolar constriction.

They compared the findings in the eyegrounds and the types of placental infarcts and found that usually both help to classify the toxemia. When the hypertension was due to vascular disease the eyegrounds usually showed evidence of arteriolar sclerosis, and the placenta, fixed in solution of formaldehyde U. S. P., usually showed white, or nontoxic, infarcts. When the hypertension was of toxic origin, the eyegrounds usually showed angiospasm and the placenta, fixed in solution of formaldehyde U. S. P., usually showed infarcts varying in color from yellow to brown and to black. The darkness of the infarct increased in proportion to the severity of the toxemia.

When hypertension is present during pregnancy without evidence of vascular or renal disease, the present consensus is that it is based on angiospasm. Addis [34] and Weiss [35] are among the most outspoken of the recent writers favoring this opinion. Many observers have seen spastic constrictions of the retinal arterioles during toxemia of pregnancy. Wagener found spastic constrictions of the arterioles in skeletal muscles taken for biopsy from patients with toxemia of pregnancy who at the same time showed spastic constrictions of the retinal arterioles. Hinselmann and associates,[36] according to Mussey, observed with the microscope recurring spasmodic constrictions of the arterioles in the nail fold of eclamptic patients.

Addis claimed that angiospasm produces the hypertension and explains all signs and symptoms of eclampsia. In the brain it produces hypertensive encephalopathy and excites convulsions; in the kidney it is responsible for albuminuria and oliguria, with a high specific gravity; in the liver it causes periportal necrosis; in the subcutaneous tissue it is responsible for anasarca, and in the skin it manifests itself by pallor.

34. Addis, W. R.: Pathogenesis of Eclampsia, Brit. M. J. **1**:1103 (May 29) 1937.

35. Weiss, E.: Practical Talks on Kidney Disease, Springfield, Ill., Charles C Thomas, Publisher, 1937, p. 138.

36. Hinselmann, H.; Neetekoven, H., and Silberbach, W.: Capillary Circulation in Eclampsia, Arch. f. Gynäk. **116**:443 (Jan.) 1923; abstracted, J. A. M. A. **80**:1108 (April 14) 1923.

Lyle [37] recently cited toxemia of pregnancy as a condition that occasionally produces encephalopathy.

The after-effects of toxemia of pregnancy have been studied by many clinicians. Peckham [38] found that the frequency of chronic nephritis following eclampsia increased in proportion to the height of the systolic blood pressure. Nephritis did not develop if the systolic pressure did not exceed 170 mm. of mercury; however, nephritis developed in 15 per cent of patients whose pressure reached 170 to 200 mm. and in 48 per cent when the pressure exceeded 200 mm.

Herrick and Tillman [39] reported a series of 188 patients with mild toxemia of pregnancy, one third of whom showed hypertension one year or more later. Peckham and Stout [40] reported a similar series, one half of whom showed chronic vascular or renal disease five years later. Stander [41] followed 800 patients, 35 per cent of whom had chronic nephritis, and 40 per cent of the latter had died in five to seven years.

Herrick and Tillman [42] followed another large series of patients with toxemia of pregnancy and found that 80 per cent of the determinable deaths were of cardiovasculorenal origin. The mortality rate of this group was nearly seven times the average death rate for women of the child-bearing age. They found that 30 per cent of a group of patients who had non-nephritic hypertensive toxemia of pregnancy had a blood pressure of 150 mm. at the end of the first year, and at the end of three years 50 per cent showed this degree of pressure, together with definite retinal arteriolar sclerosis.

CONCLUSIONS

The obstetrician should do his own ophthalmoscopy, because he will often gain invaluable information concerning the degree and severity of the toxemia, and without delay or extra expense to the patient. If this study is done only by the consultant ophthalmologist, he will be called in only once or twice in an occasional case of severe toxemia. At least 10 per cent of pregnant women show some degree of late toxemia,

37. Lyle, D. J.: Association Between Retinopathies and Encephalopathies in Common Cardiovasculo-Renal Affections, Am. J. Ophth. **27**:1232 (Nov.) 1944.

38. Peckham, C. H.: Chronic Nephritis Complicating Pregnancy, Am. J. Surg. **35**:325 (Feb.) 1937.

39. Herrick, W. W., and Tillman, A. J. B.: Mild Toxemias of Late Pregnancy: Their Relation to Cardiovascular and Renal Disease, Am. J. Obst. & Gynec. **31**:832 (May) 1936.

40. Peckham, C. H., and Stout, M. L.: Low Reserve Kidney, Am. J. Surg. **31**:92 (Jan.) 1936.

41. Stander, H. J., cited by Norton, J. F., and Connell, J. N.: Management of Toxemias of Pregnancy, J. M. Soc. New Jersey **33**:499 (Sept.) 1936.

42. Herrick, W. W., and Tillman, A. J. B.: Toxemia of Pregnancy: Its Relation to Cardiovascular and Renal Clinical and Necropsy Observations, with Long Follow-Up, Arch. Int. Med. **55**:643 (April) 1935.

according to Mussey [43]; and, in the opinion of McCord,[44] chief of the obstetric staff where this study was made, the examination of the eyegrounds by one experienced in their interpretation gives the most information concerning the management and course of the various toxemias of pregnancy.

It is now generally agreed that acute hypertensive true toxemia of pregnancy is characterized by localized and generalized spastic constriction of the arterioles, the degree of which has been found to parallel closely the severity of the toxemia. The degree of spasm of the retinal arterioles indicates the degree of angiospasm in other parts of the body. The eyegrounds should be examined routinely during the early months of pregnancy to determine the status of the arterioles, which will aid in the prognosis of the present pregnancy and will be valuable in interpreting changes that will be seen if toxemia appears later in pregnancy. When hypertension and other symptoms during late pregnancy indicate toxemia, the eyegrounds should be examined every few days, with special attention to the degree of angiospasm. When the degree of angiospasm increases in spite of conservative medical treatment, the pregnancy should be terminated to prevent permanent damage to the mother's vascular system. In some cases of toxemia the induction of labor is often a life-saving act for both mother and baby, and a study of the eyegrounds is probably the most consistently reliable single guide in determining when pregnancy should be terminated. On the other hand, the absence or scarcity of changes in the eyegrounds is often of great help in determining when it is safe to allow pregnancy to proceed.

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43. Mussey, R. D.: Significance of Retinal Changes in Toxemias of Pregnancy, M. Clin. North America **24**:1151 (July) 1940.

44. McCord, J. R.: Conservative Treatment of Eclampsia: Study of One Hundred and Forty-Eight Cases, J. M. Soc. New Jersey **34**:9 (Jan.) 1937.

OPHTHALMOSCOPIC CHANGES ASSOCIATED WITH HYPERTENSIVE VASCULAR DISEASE AS A GUIDE TO SYMPATHECTOMY

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DURING recent years many articles have been published concerning the importance of fundic changes associated with benign and malignant essential hypertension (benign and rapidly progressive hypertensive vascular disease).[1] These fundic findings will be discussed in relation to the surgical treatment of this prevalent disease. Others will discuss the surgical and medical aspects.

Essential Hypertension is regarded as a vascular disease of unknown etiology. Its main clinical manifestation is a persistent high diastolic blood pressure, with variable general symptoms. The disease often causes spasm or sclerotic thickening of the walls of the retinal choroidal arterioles. This results in narrowing or stenosis of the lumen, which frequently leads to pathologic changes in the surrounding area.

Essential hypertension may be divided into two forms: benign and malignant. The benign form is a chronic disease; the malignant form is an acute disease. Both forms occur mainly in adults. Occasionally the benign form may become malignant, in which case fundic lesions are extensive.

The fundic changes occurring with essential hypertension are varied. Sometimes the fundi are normal for many years and no treatment

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From the Department of Surgery of the New York Post-Graduate Medical School and Hospital (Columbia University).

1. Cohen, M.: Significance of Pathologic Changes in Fundus in General Arterial and Kidney Diseases, J. A. M. A. **78**:1694-1698 (June 3) 1922; Chorioretinal Arteriolar Necrosis in Malignant Hypertension, Arch. Ophth. **23**:1052-1058 (May) 1940. Gans, J. A.: Classification of the Arteriosclerotic-Hypertensive Fundus Oculi in Patients Treated with Sympathectomy, ibid. **32**:267-275 (Oct.) 1944. Hinton, J. W., and Lord, J. W.: The Surgical Treatment of Advanced Hypertension, New York State J. Med. **1**:13-17 (Aug. 20) 1945. Moritz, A. R., and Oldt, M. R.: Arteriolar Sclerosis in Hypertensive and Non-Hypertensive Individuals, Am. J. Path. **15**:679-728 (Sept.) 1937. Smithwick, R. H.: Experiences with Surgical Treatment of Hypertensive Cardiovascular Disease of Man, Cleveland Clin. Quart. **12**:105-117 (Oct.) 1945. Wagener, H. P.; Cusick, P. L., and Craig, W. M.: The Retina in Surgical Cases of Primary Hypertension, Tr. Am. Ophth. Soc. **37**:379-394, 1939. Peet, M. M.; Woods, W. W., and Braden, S.: Surgical Treatment of Hypertension, J. A. M. A. **115**:1875-1885 (Nov. 30) 1940. Woods, W. W., and Peet, M. M.: The Surgical Treatment of Hypertension, ibid. **117**:1508-1515 (Nov. 1) 1941.

beyond general medical care may be required. At other times the fundi may show mild, moderate or severe lesions. For a time these changes may be stationary, progressive, regressive or remittent. A definite prognosis is not possible from the fundic findings alone, as it may be influenced by pathologic changes in other organs. Still, the eyegrounds are the best visible guide available to the condition of the systemic blood vessels, and therefore ophthalmoscopic findings afford an important prognostic indication in cases of essential hypertension.

Various systemic diseases may be accompanied with fundic lesions similar to those observed with essential hypertension. Accordingly, a physical examination should be made, and a clinical history and laboratory reports should accompany the fundic findings in order to establish a clinical diagnosis. Essential hypertension presents no pathognomonic signs; therefore, no definite correlation between the fundic findings and the unknown factor causing essential hypertension can be established.

Retinal lesions associated with benign essential hypertension are not inflammatory; hence, they are known as retinopathies or neuroretinopathies. Fundic lesions may be present in one or both eyes and may affect one eye more than the other. The acuity of vision will not be seriously involved unless the macular area or the visual field is affected.

Ophthalmoscopic diagnosis in cases of hypertensive disease requires a differentiation between arteriolar spasm and arteriolar sclerosis, which is an important but frequently impossible distinction. Some of the distinguishing fundic signs in spasm are retinal venous engorgement with tortuosity; narrowed arterioles, at times showing an uneven caliber; edema of the disk and retina; retinal hemorrhages and cotton wool patches, clinically recognized as exudates, and perivasculitis. These findings are usually transient and disappear with a period of absolute rest and the use of vascular dilators and sedatives.

If the narrowed arterioles are sclerotic, the vascular lesions are frequently permanent. The arterioles remain contracted; some have a "silver wire" central light reflex, while others are invisible, due to extreme contraction, or may be replaced by whitish lines, as in endarteritis. The venules are congested and tortuous and are compressed and deflected where crossed by sclerosed arterioles. There are retinal edema, hemorrhages and exudates. The exudates are usually resorbed in a short time; the glistening whitish dots or fatty degenerations remain for a long period.

Secondary hypertension will not be discussed, since it is caused by known primary disease entities, such as toxemia of pregnancy, pyelonephritis, chronic glomerular nephritis, tumor of the adrenal gland and arteriosclerosis. In cases of the secondary type treatment of the primary disease is necessary.

PRESENT STUDY

Through the courtesy of Dr. J. William Hinton, it was my privilege to examine the fundi of 90 patients with essential hypertension who were to undergo surgical treatment at the New York Post-Graduate Hospital. The fundi were examined frequently before and after operation over periods ranging from several months to two years. The findings were recorded and checked with other clinical data. Patients with severe organic disease were excluded.

Each patient was required to remain one or two weeks in the hospital prior to thoracolumbar sympathectomy in order to study the effects of rest and of the sodium amytal test on the diastolic pressure, as well as the data supplied by the physical examinations, including roentgenologic and electrocardiographic studies and laboratory tests of the blood and urine. If these reports proved satisfactory, the operation was performed in two stages at intervals of ten to fourteen days. For a detailed description of the operative technic it is necessary to consult surgical publications. Biopsies of small sections of the renal cortex were made at the second operation and were examined histologically.

According to my ophthalmoscopic findings, the fundi of patients with essential hypertension may be normal or the lesions may be classified as mild, moderate and severe. This is a tentative grouping and cannot be considered a hard and fixed distinction, as there are many borderline lesions. The results of successive examinations frequently determine their actual grading.

Of the 90 patients with essential hypertension, 86 revealed either normal fundi or mild or moderate fundic lesions, while 4 patients had severe lesions, such as occur with malignant essential hypertension.

Twenty-three patients had normal fundi, possibly because they were in an early stage of the hypertensive disease. One patient refused to undergo operation. The postoperative findings in the fundi of the remaining 22 patients continued to be normal. Microscopic examination of sections of the kidney showed normal structure in 3 patients, while 19 had mild or moderate nephrosclerosis of the interlobular renal vessels. Ophthalmoscopic examination served as a guide for sympathectomy in this group of patients, as it showed no evidence of the diffuse arteriolar disease, thereby suggesting a favorable prognosis. Sympathectomy was performed in order to relieve the severe subjective symptoms of these patients. The high diastolic blood pressure after sympathectomy was reduced in all but 2 patients in six months.

Fundic changes classified as mild were present in 43 patients. Most of these fundi showed a preoperative contraction of some arterioles with prominence of the central light reflex; the retinal veins were moderately engorged and tortuous, with compression over some arteriolar crossings; at times a few small hemorrhages and exudates were visible. One patient refused to undergo operation. Ten patients had normal fundi after operation; these fundi had shown spastic arteriolar lesions before operation. Thirty-two patients showed postoperative signs of arteriolar

sclerosis, consisting of a retinal residue of moderate venous engorgement, with local compression, and prominence of the central light reflex in the arterioles. These vascular changes were not reversible, but the edema, hemorrhages and exudates were resorbed after several days or a few weeks, contrary to similar lesions in cases of nonhypertensive diseases in which absorption occurs after longer periods. In all these patients biopsy of the kidney revealed mild or moderate nephrosclerosis. In this group of patients the ophthalmoscopic examination served as a guide for sympathectomy by the recognition of the early phase of the hypertensive vascular disease. Six months after sympathectomy the high diastolic blood pressure was greatly reduced in all but 5 patients. One patient in this group died of coronary disease two days after operation.

In the 20 patients with moderate fundic lesions before operation, the retinal arterioles showed a silvery white central light reflex; some venules were congested, with local compression and deflection, and there were slight edema of the disk, small edematous retinal areas, diffuse hemorrhages and exudates. One of the patients in this group refused to have an operation, and 1 was excluded because of organic disease. Two of the patients with preoperative angiospasm showed normal eyegrounds after operation, while in 16 there remained a residue of retinal arteriolar sclerosis. Within two days after operation 3 patients had fresh retinal hemorrhages and exudates, which, however, were transient. In this group with moderate hypertension the findings again indicated that the basic vascular lesions were not reversible, but the edema, hemorrhages and exudates were all resorbed. The sections of the kidney all indicated mild or moderate nephosclerosis. In cases of moderate lesions of the eyegrounds, sympathectomy was indicated in order to prevent a possible progression to an advanced phase of the hypertensive disease. The high diastolic pressure in this group was greatly reduced six months after sympathectomy in all but 5 patients. Of 2 patients whose pressure was not reduced, 1 died of coronary disease four months and the other eight months after sympathectomy.

The fundic lesions in the 4 patients with severe, or so-called malignant, hypertension were extensive. The retina showed very severe lesions; as in the patients with moderate hypertension, there were massive areas of retinal edema with or without papilledema, profuse hemorrhages, a partial or complete star-shaped figure in the macular area, thromboses and exudates. These lesions signified the advanced phase of essential hypertension and generally indicated involvement of a vital organ. Two patients were not operated on because of concomitant organic disease. One patient died shortly after operation of a tumor of the adrenal, and 1 of coronary occlusion one month after operation. Biopsy revealed malignant nephrosclerosis of the kidney in 1 of the patients undergoing operation and moderate vascular involvement in

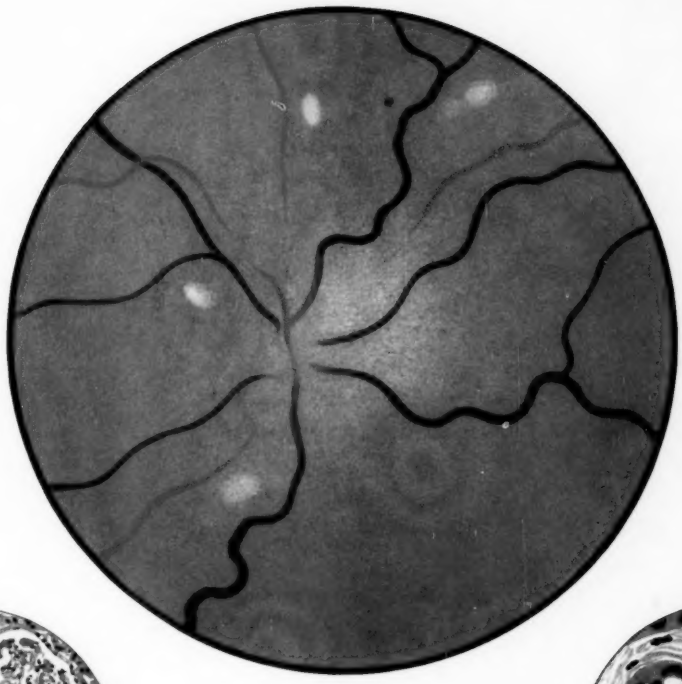

Fig. 1.

Fig. 3.

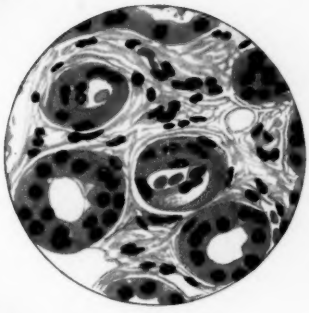

Fig. 4.

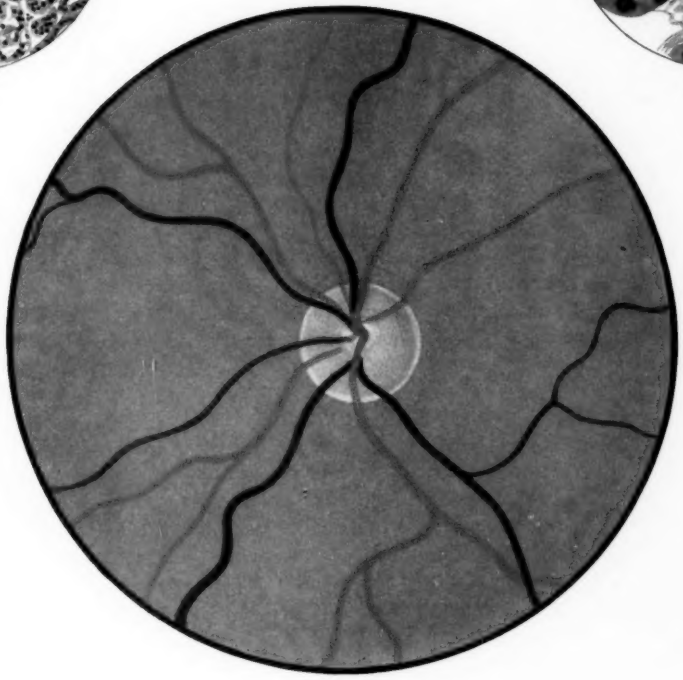

Fig. 2.

Fig. 1. Before Sympathectomy
Fig. 2. Three weeks after Sympathectomy
Fig. 3. Kidney Section (Low Power)
Fig. 4. Kidney Section (High Power)

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the other. From an ophthalmoscopic standpoint, sympathectomy in cases of severe hypertension would be advisable only if the patient insisted on it because of suffering from severe subjective symptoms which medical treatment could not alleviate.

In this connection, I have reported a case of so-called malignant essential hypertension with severe fundic lesions in which death was due to cerebral hemorrhage. Pathologic study demonstrated necrosis of the arteriolar wall of the retina and choroid and hyperplastic arteriolar sclerosis in all the organs, as verified by autopsy. I have observed a few patients with severe fundic lesions associated with malignant hypertension for several years; they lived from two to eight years without surgical intervention. However, satisfactory results have been reported after sympathectomy in cases of malignant hypertension with severe fundic lesions.

It is important to note that in the majority of the 90 patients the progression of clinical manifestations of the hypertensive disease was reflected in progression of the fundic lesions. The association of the fundic findings with renal arteriolar sclerosis is significant; it was manifested in 96 per cent of the patients operated on. This fact requires further investigation as to prognosis.

The following case is 1 of several in which the ophthalmoscopic findings served as an important guide to thoracolumbar sympathectomy.

REPORT OF A CASE

L. D., a man aged 34, white, single, was a newspaper deliverer. His family history was irrelevant, and he had been in perfect physical health until 1941. At this time his draft board diagnosed his physical condition as ideopathic hypertension. He then was treated by his family physician for this ailment for two years. Medical treatment was of no avail in relieving his symptoms. His blood pressure gradually rose to 250 systolic and 150 diastolic, and he had excruciating headaches and other subjective complaints. He was referred to Dr. Maurice Bruger, who, in turn, suggested that he be admitted to the New York Post-Graduate Hospital for sympathectomy. On his admission in June 1943, the nonprotein nitrogen was 35 mg., and the urea nitrogen 17.5 mg., per hundred cubic centimeters; the test for urea clearance, as well as other tests, gave normal results. Examination of the fundi showed a moderate form of neuroretinopathy (fig. 1).

He was admitted to the hospital, and after a two week period for preliminary examinations, the results of which were satisfactory, a thoracolumbar sympathectomy was performed by Dr. J. William Hinton. Postoperative results were satisfactory; his blood pressure was reduced to an average of 150 systolic and 100 diastolic; his headaches disappeared completely, and he was able to resume his work after an absence of five months. For a period of two years his condition has remained satisfactory, and he is at present in perfect health.

He has had periodic ophthalmoscopic examinations for the past two years. Postoperative examinations of the fundi showed resorption of all retinal lesions, with a normal vasculature after three weeks (fig. 2). The angiospastic condition

which existed prior to operation was relieved. No evidence of angiosclerosis was seen at any time in the fundi. Biopsy of the kidney revealed mild nephrosclerosis, demonstrating hyaline thickening of the intima and media of the arterioles (figs. 3 and 4). This case exemplifies the beneficial and satisfactory results obtained from thoracolumbar sympathectimy.

SUMMARY AND CONCLUSIONS

In 82 patients with benign essential hypertension (hypertensive vascular disease) no progression of the retinal lesions was observed after sympathectomy.

Of 60 patients with associated hypertension with mild or moderate fundic lesions, regression of the retinal hemorrhages, exudates and edema were observed in 22 after sympathectomy; but the basic underlying retinal arteriolar sclerosis remained unchanged in 48. Retinal angiospasm was relieved in 12 patients. Further study is required to determine the significance of this retinal residue.

Cases of benign essential hypertension, showing normal eyegrounds or mild or moderate fundic lesions, are suitable for sympathectomy if continued medical treatment is of no avail in alleviating the severe and persisting subjective symptoms.

The group of patients who had so-called malignant (rapidly progressive) hypertension with extensive fundic lesions was too small to call forth any comment. An adequate series of such patients should be studied from an ophthalmoscopic standpoint.

Finally, the purpose of sympathectomy is the relief of subjective symptoms of patients with essential hypertension. The advisability of sympathectomy is determined primarily by the internist, whose decision is based on the consideration of all clinical data in essential hypertension.

29 East Sixty-Fourth Street.

KERATOCONJUNCTIVITIS DUE TO A DIPHTHEROID-LIKE ORGANISM

Report of a Case

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AND
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NUMEROUS organisms and infectious agents have been implicated in keratoconjunctivitis. The following case illustrates a severe type of infection produced by an organism of the diphtheroid group.

REPORT OF CASE

History.—M. A. V., a 26 year old unmarried white woman, was first seen at the Institute of Ophthalmology on March 21, 1944, with the following history. At the age of 7 she had an attack of scarlet fever, which left her eyes sensitive to light for about one year. There was, however, no other ocular complaint until six years prior to the first examination, when, rather suddenly, severe blepharoconjunctivitis developed in both eyes. This condition was treated with drops by several doctors, and there were numerous exacerbations and remissions. There was considerable purulent discharge, and the patient stated that the margins of the lids remained red and irritated. In 1940 she noted a decrease in visual acuity, especially in the right eye. There was increased sensation of irritation; the eyes were acutely inflamed, and she was told that her corneas were scarred. At the same time she began to be troubled with trichiasis, for which frequent epilation was necessary. There was no history of a diagnosis of trachoma having been made, nor was there any history of physical illness.

Examination.—Vision was 3/200 in the right eye and 20/70 in the left eye with and without correction. She was wearing + 3.00 D. cyl., ax. 95 for the right eye and + 0.50 D. sph. ⊃ — 2.50 D. cyl., ax. 5 for the left eye. There was considerable injection of the bulbar conjunctiva, especially at the inner canthus. The normal mucocutaneous juncture of the lids was obliterated and was replaced by scar tissue, containing a large number of aberrant cilia, especially on the lower lids. This scar tissue was about 4 mm. wide and extended as a ragged edge over onto the conjunctival surface of the lids. There were redness and roughening of both the upper and the lower fornix, with papillary hypertrophy. In the regions of the upper tarsus were some follicles and a minimum amount of scarring.

Examination of the right eye with the corneal microscope revealed a thin vascularized membrane over the entire cornea with small areas of calcification in the center (fig. 1). There was some punctate staining around the calcified areas. The left eye showed considerable punctate staining with fluorescein and an

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area of vascularization invading the limbus 2 or 3 mm. and extending clockwise from 6 to 2 o'clock. The border of this area did not stain, however.

The tension of the two eyes was normal to finger palpation. Ophthalmoscopic examination was unsatisfactory in the right eye because of the corneal opacification. The left fundus was normal.

The appearance of the eyes suggested an eczematous (scrofulous, phlyctenular or lymphatic) conjunctivitis with associated corneal changes and an old ulcerative blepharitis with no phlyctenules present now. The pannus also suggested this diagnosis rather than that of trachoma, since the vascularization was not confined to the upper portion of the cornea.

General examination revealed a somewhat undernourished condition. Studies of the blood revealed a hemoglobin concentration of 73 per cent and a red cell count of 3,570,000. The white cell count was 5,000, with 57 per cent polymorphonuclear cells and 40 per cent lymphocytes. She was given vitamin B complex, oral liver extract and elixir of a proprietary hematinic preparation (Feosol). Under this treatment her appetite improved and she felt stronger.

Cultures were taken of the eyes, and epilation was done. She was given an ointment containing sodium sulfathiazole, 5 per cent, to instill in the eyes three times a day.

LABORATORY STUDIES

Morphologic Characteristics.—Cultures taken from the conjunctivas and lids of both eyes revealed a pure culture of a gram-positive bacillus which was isolated from aerobic and anaerobic conditions. Direct smears from the conjunctivas showed a moderate number of gram-positive, diphtheroid-like organisms with short and long forms. Also present were a moderate number of polymorphonuclear leukocytes and a few epithelial cells. No inclusion bodies were observed in epithelial scrapings stained with the Giemsa stain. The diphtheroid-like organisms showed considerable pleomorphism. Some were in the form of parallel rods; others had club-shaped ends. No capsule was observed. Granules were noted and were more prominent when stained with methylene blue. The organisms were nonmotile and non-acid-fast. A few staphylococci were also present which did not ferment a phenol red (phenolsulfonphthalein)–mannitol agar plate.

Cultural Characteristics.—Growth was obtained on ordinary mediums of material taken directly from the eye. On plain agar the colonies developed gradually from 1 to 5 mm. after seventy-two hours' incubation at 37 C. The optimum temperature for growth was 37 C., but the bacteria grew at room temperature. In older cultures, after four to five days, a yellow pigment developed. The colonies appeared rough, irregular and dry, with grayish margins and yellow centers (fig. 2). They were not convoluted and were easily dislodged from the medium. The same morphologic features were noted on a rabbit blood agar plate, and there was no hemolysis. On potato medium a scant growth was obtained in forty-eight hours. In liquid mediums after twenty-four hours a pellicle formed, which broke up into small flakes. This pellicle was yellow.

Resistance.—The culture survived without subculturing for about nine months. Broth cultures heated at 56 C. for one hour produced no growth.

Biochemical Reactions.—The organisms produced acid without gas with dextrose, maltose, sucrose, levulose and xylose. With raffinose acid was produced in twenty-four hours, but the reaction was reversed to neutral after forty-eight hours. No acid or gas was produced with salicin, dulcite, mannitol or lactose (table 1). In litmus milk a very slight acidity was produced after incubation

for one week. No coagulation or digestion occurred after incubation for two weeks. Gelatin and Löffler's medium were not liquefied. The methyl red test gave a negative reaction, and no indol or hydrogen sulfate was produced. Nitrites were not formed.

Animal Inoculation.—An emulsified culture of the isolated bacillus was prepared and the following animal inoculations were carried out:

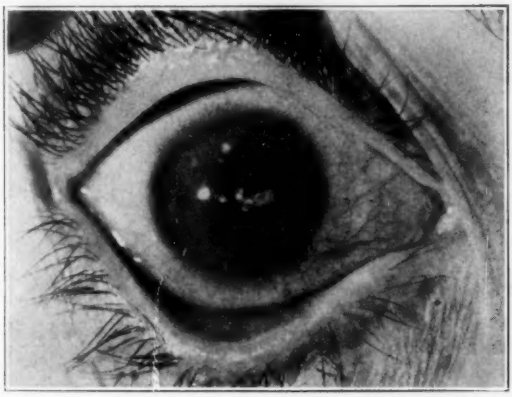

Fig. 1.—Vascularized membrane covering cornea, with areas of calcification.

Mouse: An intraperitoneal injection of 0.3 cc. of the emulsified broth culture was made, using an adult white mouse. No effect was produced in two weeks.

Guinea Pig: An intraperitoneal injection of 0.3 cc. was made, with no effect.

Rabbit: An adult white rabbit was used for intraocular studies. The right eye was given a subconjunctival injection of 0.05 cc. of the broth culture,

TABLE 1.—*Biochemical Reactions of Fermentation Sugars*

Fermentation Sugars	Acid	Gas
Dextrose	+	0
Maltose	+	0
Sucrose	+	0
Levulose	+	0
Raffinose	+ (after 24 hr.)	0
Xylose	+	0
Salicin	0	0
Dulcite	0	0
Mannitol	0	0
Lactose	0	0

the point of injection being just above the limbus at 12 o'clock. The following day the entire cornea was greatly injected, and there was a purulent discharge containing the organisms. At the end of a week the conjunctival reaction subsided, but there was now a beginning vascularization of the cornea above and below (fig. 3*A*).

An injection was made in the other eye of the same rabbit, using 0.02 cc. of the emulsified broth culture, the injection being made through the cornea into

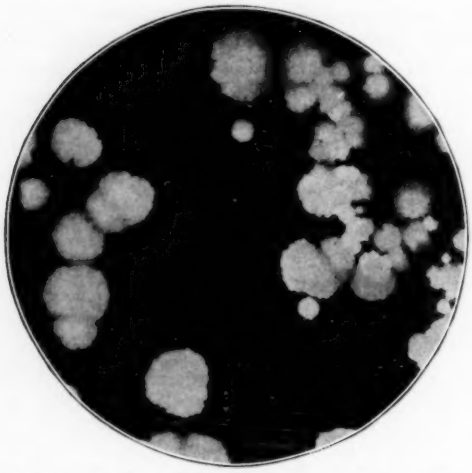

Fig. 2.—Colonies of Corynebacterium xerose four to five days old.

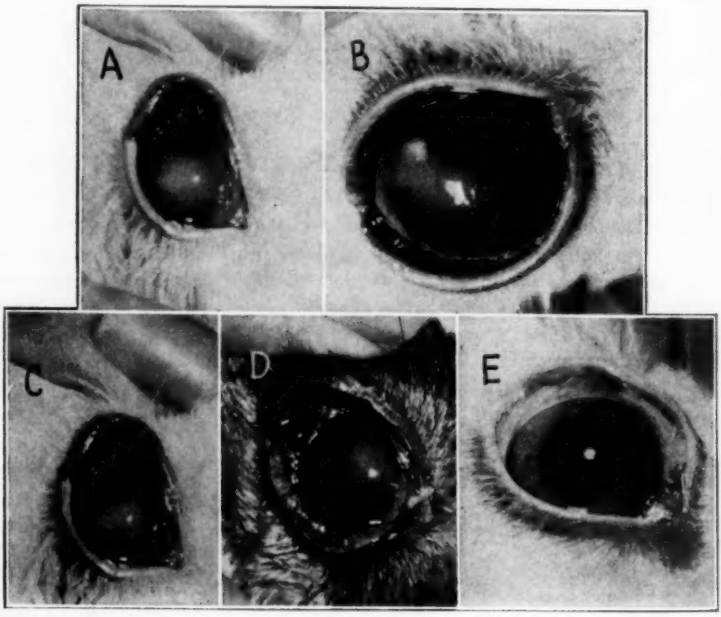

Fig. 3.—Rabbit eyes after injection of a broth culture of the diphtheroid organism taken from the eye shown in figure 1. *A*, beginning vascularization of the cornea one week after subconjunctival injection of 0.05 cc. of the broth culture just above the limbus; *B*, opaque, vascularized cornea about three weeks after injection of 0.02 cc. of the broth culture into the anterior chamber of the other eye of the same rabbit; *C*, cloudy cornea of a second rabbit twelve days after injection into the anterior chamber of 0.04 cc. of another broth culture of the organism; *D*, complete opacification of the cornea and conjunctivitis in a third rabbit two weeks after injection into the anterior chamber of 0.02 cc. of the same culture as that given the second rabbit; *E*, rabbit eye into which a plain sterile broth was injected, as a control.

the anterior chamber. The following day the conjunctiva was found to be greatly congested, with purulent discharge. The anterior chamber was reformed; the cornea was somewhat translucent, and the tension was normal to finger palpation. Four days later a thick exudate was noted in the anterior chamber. At the end of a week the cornea was hazy. At the end of two weeks the conjunctival reaction had subsided. The cornea was now completely opaque and vascularized (fig. 3 *B*). Tension as taken with the fingers appeared low. There was no change in appearance at the end of three weeks. Another rabbit received an injection of 0.04 cc. of another broth preparation of organisms into the anterior chamber. At the end of eight days a pannus had formed from above, and there was considerable reaction in the conjunctiva, which subsided at the end of twelve days, leaving a cloudy cornea (fig. 3 *C*).

An additional rabbit was given an injection of 0.2 cc. of the same broth culture. The following day there was a severe purulent conjunctivitis containing the same organisms, as well as staphylococci. At the end of two weeks there was complete opacification of the cornea, with considerable conjunctivitis still remaining (fig. 3 *D*). Tension as taken with fingers was low.

Scrapings were taken from the lower lids on Jan. 30, 1946 and placed in a test tube of saline solution. An injection of 0.02 cc. was made in the anterior chamber of a rabbit. The effect produced was similar to that shown in figure 3 *C*.

Two rabbits received injections of 0.02 cc. of saline solution and broth, respectively, in their right eyes. No effect was produced. Figure 3 *E* shows the rabbit's eye after injection with plain sterile broth.

Monkey: A few drops of a broth culture of the organisms was instilled in the right eye of a Macacus rhesus monkey. The following day there was a slight redness of the conjunctiva, which disappeared within twenty-four hours.

Clinical Course.—The patient was advised to use sodium sulfathiazole ointment, five per cent, three times a day, and epilation was done at intervals of two weeks to cut down irritation to the cornea. In addition, she received an extract of liver and iron by mouth and was placed under the care of an internist. The cornea ceased to stain after two weeks, and vision improved.

On Oct. 19, 1944 vision in the right eye was 20/200—, not improved, and in the left eye was 20/30, corrected to 20/20–1 with a + 0.25 D. sph ⌒ –2.50 D. cyl., ax. 15. Examination with the slit lamp showed considerable clearing of the left eye but with the vascularization and calcified deposits remaining. The left eye showed thinning of its vascularized area. There was no staining of either eye after two weeks of treatment. On March 1, 1945 the hemoglobin had risen to 92 per cent and the red cell count had reached 4,355,000.

Cultures have remained positive in spite of the clinical improvement. Penicillin ointment has been tried, and at present the patient uses this twice a day and alternates with the sodium sulfathiazole ointment at monthly intervals. There are fewer abnormal cilia now, and the patient has less irritation as long as she continues to use local applications of ointment to the eyes. Vision in the right eye is now corrected to 20/100 with + 3.00 D. cyl., ax. 95, and vision in the left eye is 20/20 with the previous correction.

Cultures from both eyes still produce heavy growths of the organisms in spite of local chemotherapy. There continue to be considerable injection and roughening of the conjunctival surfaces of the lids.

CONCLUSIONS

In view of our bacteriologic studies, we feel that the etiologic factor in this case is the diphtheroid-like organisms which we have isolated in pure culture. Biochemical reactions would place it with the diphtheroid type of the Corynebacterium group (table 1). A comparison of this organism with other diphtheroids (table 2) would lead one to consider it in the Corynebacterium xerose group. The fact that the organism was nonpathogenic for mice and guinea pigs would rule out the possibility of its being Corynebacterium pseudotuberculosis ovis (of Preisz and Nocard) or Corynebacterium pseudotuberculosis murium, both of which produce systemic effects when injected intraperitoneally into such animals. It could be a form of Corynebacterium flavidum, which is found in the nose and throat and which also occurs in the udder of cows with mastitis.

TABLE 2.—*Differentiation of the Various Forms of Corynebacterium*
(Adapted from Topley and Wilson)

	Fermentation of Sugar						Liquefaction of Gelatin
	Dextrose	Maltose	Saccharose	Dextrin	Lactose	Mannitol	
C. diphtheriae	+	+	−	+	−	−	−
C. diphtheriae (avirulent)	+	+	−	+	−	−	−
C. hoffmanni	−	−	−	−	−	−	−
C. xerose	+	+	+	−	−	−	−
C. pyogenes	+	+	+?	−?	±	−	±
C. renale	+	−	−	−	−	−	−
C. ovis	+	+	−	±	−	−	+
C. murium	+	+	+	−	−	−	−
C. acnes	+	+	±	−?	−	+	−
C. typhi	+	+	−	−	−	−	−

During the past fifty years considerable work has been done in an attempt to prove the pathogenicity or nonpathogenicity of C. xerose. Fränkel and Franke [1] in 1887 injected material containing C. xerose organisms into the anterior chamber of the guinea pig and instilled the same material into the conjunctival sac of 5 human subjects, with no untoward results. Weeks [2] in 1887 made a study of the xerosis bacillus in infants and children and came to the conclusion that no pathologic change was produced.

Bietti [3] in 1903 carried out studies in which he inoculated the eyes of several of his colleagues, with no ill effects. Andrewes, Bulloch and

1. Fränkel, E., and Franke, E.: Ueber den Xerosebacillus und seine ätiologische Bedeutung, Arch. f. Augenh. **17**:176-192, 1887.

2. Weeks, J. E.: Xerosis conjunctivae bei Säuglingen und bei Kindern, Arch. f. Augenh. **17**:193-202, 1887.

3. Bietti, A.: Welche Bedeutung kommt den Diphtheriebazillen und verwandten Keimen in der Aetiologie der einfachen Bindehautentzündungen zu? Klin. Monatsbl. f. Augenh. **41**:87-124, 1903.

others [4] reported a series of studies in 1923 with the same results. Gay,[5] Topley and Wilson [6] and Duke-Elder [7] all stated that there is no adequate evidence that the diphtheroids are pathogenic for the eye.

It is our feeling that the organism isolated in this case is a diphtheroid. In spite of statements to the contrary, it would seem as though this organism was pathogenic. This is especially true since no organisms of the Haemophilus group were found in the patient's eyes. The point might be raised that there is a history of poor physical condition, such as might cause nutritional changes in the cornea. In view of the improvement in the patient's physical condition and the continued infection with exacerbations and remissions, we feel that the organism described has a direct relationship to the keratoconjunctivitis.

SUMMARY

A stubborn case of keratoconjunctivitis with blepharitis and trichiasis is presented in which a pure culture of a diphtheroid-like organism was isolated.

Dr. Martin Frobisher, of Johns Hopkins University, and Dr. Harry E. Martin, of the University of Pennsylvania, assisted in identifying the organisms isolated in this case.

635 West One Hundred and Sixty-Fifth Street.

4. Andrewes, F. W., and others: A System of Bacteriology in Relation to Medicine, Medical Research Council, London, His Majesty's Stationery Office, 1923, p. 380.

5. Gay, F. P.: Agents of Disease and Host Resistance, Springfield, Ill., Charles C Thomas, Publisher, 1935, pp. 948-951.

6. Topley, W. W. C., and Wilson, G. S.: The Principles of Bacteriology and Immunity, Baltimore, William Wood & Company, 1936, pp. 346-551.

7. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 2, pp. 1467-1468.

SENSORIAL RETINAL RELATIONSHIP IN CONCOMITANT STRABISMUS

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(Continued from Page 368).

III. CLINICAL PICTURE OF ANOMALOUS RETINAL CORRESPONDENCE AND ITS INTERPRETATION

The normal relationship between the two retinas, the normal retinal correspondence, is based anatomically on the interrelation between the cells of the sensory epithelium of the retinas and the cells of the visual sphere of the brain cortex. Ample experimental evidence has shown that the normal retinal relationship is physiologically fixed and that it cannot be altered in a subject with normal binocular vision. Yet anomalous correspondence does exist and can be observed daily in the practice of every ophthalmologist.

How can this apparent contradiction be explained? The supporters of the so-called empiristic theory of space perception found an easy solution to this problem and, indeed, perceived one of the foundations of their doctrine in the fact that squinting persons are capable of acquiring a retinal relationship which differs from that of nonsquinters. They reasoned that the faculty of localizing bifoveal stimuli in the same direction is learned and acquired in the early stages of individual life. However, such a type of localization is useful only if the visual lines intersect at the point of fixation. If there is a deviation of one of the visual lines, that is, if there is a strabismus, the patient makes up for the motor anomaly by learning how to localize in the same relative direction a stimulus impinging simultaneously on the fovea of one retina and on an eccentric element of the other retina; i. e., he acquires anomalous correspondence.

The empiristic theory has been superseded by the nativistic theory, according to which the normal retinal correspondence is innate or acquired through phylogenetic, rather than individual, experience. Every one is born with such a distribution of the relative directional spatial values of the retinal elements that the two foveas are corresponding elements. This condition is, indeed, fixed and immutable.

It is of interest to recall in this connection Lorente de Nó's theoretic consideration of the point to point relationship between the retina and

the cerebral cortex in the region of the calcarine fissure.[39] Owing to the extensive arborization, each element of the retina is connected with a large area of the cortex, and each impulse set in any point of the retina could, therefore, be transmitted to a large area of the cortex. This overlapping of the nerve paths would make a point to point projection of the retina in the optic centers impossible if the theory of "avalanche conduction" of Ramón y Cajal and Herrick were correct. Lorente de Nó did not accept this theory. He considered the anatomic mechanism to be only potential and expressed the belief that, owing to the high threshold of the neurons, only a limited number of the anatomically possible transmission paths are accessible to afferent impulses. The role of the central stations would thus consist in concentrating the stimuli in a few conductors, rather than in increasing the number of active conductors. Physiologically, therefore, a point to point projection is possible, provided that the nerve cells have a sufficiently high threshold and are made to discharge only when a large number of their synapses are active.

It would, however, show a lack of biologic and physiologic understanding if one were to assume that a rigid anatomic point to point relationship between the elements of the two retinas would entail an equally rigid physiologic relationship.

The retina is ontogenetically, structurally and functionally a part of the brain. The prime function of the central nervous system is to correlate and integrate the activities of the organism into a purposeful unit. A rigid immutability, such as is necessary for the functioning of the peripheral organs, would defeat the purpose of the central nervous system. Its purpose is to adjust the function of the different organs and their parts in such a way as to meet the external and internal conditions present at a given moment; it must reintegrate their function if the integration is at fault or endangered. This coordinative, integrative action of the central nervous system (Sherrington[4]) is the basis of the adaptability of the human organism.

The fixed normal correspondence does not imply a true point to point relationship of the retinal elements. This would not be expedient and is not assumed in the classic writings on retinal correspondence. Johannes von Müller's old theory of the identity of the corresponding elements might, to be sure, imply such a relation, but it has long since been abandoned. It is known from Panum's investigations that the elements of each retina correspond physiologically not to one element of the other retina, but to a group of elements occupying an area of measurable dimensions. It is of importance to know that the size of

39. Lorente de Nó, R.: Studies on the Structure of the Cerebral Cortex: II. Continuation of the Study of the Ammonic System, J. f. Psychol. u. Neurol. **46**:113, 1934.

these areas is not absolutely fixed. Their dimensions are relative ones and can be somewhat reduced by training.[40]

If there is a change in the normal motor relation between the two eyes, the normal sensorial correspondence no longer serves a useful purpose; in fact, it becomes detrimental. An adjustment takes place, and a new sensorial relationship between the elements of the two retinas appears. But one must always keep in mind that the normal retinal relationship is not irretrievably lost; it remains potentially—and sometimes even actually—present; it has only given way to a new relationship, which, in turn, may be replaced if it is no longer adequate.

The anomalous sensorial relationship between the two retinas, the anomalous retinal correspondence, represents, thus, a process of adaptation of the sensorial to the anomalous motor conditions; it consists in a shift of the visual directions of one eye relative to those of the other eye.

But one cannot exact from anomalous correspondence the same accuracy as from normal correspondence. It must again be stressed that anomalous correspondence is nothing but an attempt of the organism to adapt the sensorial to the motor conditions, an attempt which is not always successful. And even where it is most successful—as in patients who in the clinical tests show an anomalous correspondence adapted to the angle of squint—refined laboratory methods may disclose considerable inaccuracies in the new sensorial relation of the two retinas. This is only to be expected, given the nature of anomalous correspondence; if one loses sight of its nature, one is apt to draw from laboratory experiments fallacious conclusions about the essence of the condition.

Not in all patients with concomitant strabismus does anomalous correspondence develop. The conditions which are necessary to bring this about must now be considered.

The first prerequisite is a certain amount of binocular cooperation. I have shown in an earlier paper that anomalous correspondence does not appear in patients whose binocular cooperation prior to the onset of the strabismus was restricted to the presence of the primitive, rudimentary visual directions.[15] The *raison d'etre* of anomalous correspondence is the binocular cooperation, and it can arise only if the eyes are, at least at times, used together. In cases of definite alternating strabismus, in which the patient is able to change fixation at will from one eye to the other and in which there is habitually alternating uniocular vision, one therefore finds normal correspondence frequently, even

40. Fischer, F. P.: Experimentelle Beiträge zum Begriff der Sehrichtungsgemeinschaft der Netzhäute auf Grund der binokularen Noniusmethode, Arch. f. d. ges. Physiol. **204**:234, 1924. Ames, A., Jr.; Ogle, K. N., and Gliddon, G. H.: Corresponding Retinal Points, the Horopter and Size and Shape of Ocular Images, J. Optic. Soc. America **22**:538, 1932. Brecher, G. A.: Form und Ausdehnung der Panumschen Areale bei fovealem Sehen, Arch. f. d. ges. Physiol. **246**:315, 1942.

though the strabismus may have begun in infancy. On the other hand, if the strabismus is purely unilateral and of long standing, the retinal correspondence is almost always anomalous. However, if one forces such a patient to fixate with the usually deviated eye, one may suddenly find that he localizes according to normal correspondence. This can be explained by the fact that anomalous correspondence is established on the basis of the usage of the eyes. If the patient is forced to use his eyes in a way unusual for him, the innate, normal correspondence will at once come into play. The situation is similar in the aforementioned cases of facultative divergent strabismus, in which the patients show a normal sensorial reaction when there is binocular fixation but anomalous correspondence when the eyes are dissociated.

In general, one can state the rule that the more unstable the motor condition is, the less stable is the sensorial reaction. The visual acuity plays no, or only a minor, role, and even a high amblyopia ex anopsia will not prevent the appearance of an anomalous correspondence.

Another factor which has to be considered is the individual difference in adaptability. Not all persons are equally well able to make adjustments, and young persons are generally more adaptable than older ones. This may explain why anomalous correspondence is found more frequently in cases in which the strabismus began early in life.

One must, furthermore, bear in mind that anomalous correspondence is a process which requires time—more time in people with low adaptability, less time in people with high adaptability. It will depend, therefore, largely on the time elapsed since the onset of the strabismus or since a change in the motor condition occurred under the influence of therapeutic measures (glasses, operations, orthoptic exercises) whether normal or anomalous correspondence, or both, will be found.

It must, finally, be reemphasized that the type of sensorial reaction elicited in the examination is also determined by the type of test used and by the way in which it is administered.

The clinical picture of the sensorial retinal relationship in concomitant strabismus is a varied one; the results of the tests in the individual case depend on all the factors which have just been discussed. These factors which influence the establishing of anomalous retinal correspondence and its clinical determination may be summarized as follows: (1) the stage of the development of binocular vision prior to the onset of the strabismus; (2) the type and stability of the motor anomaly (i. e., the use made by the patient of his eyes in ordinary life); (3) the patient's individual adaptability and his age at the time of the onset of the strabismus; (4) the time elapsed since the strabismus became manifest or since therapeutic measures affecting the angle of squint were instituted, and (5) the type of test used and the way in which it was administered.

I shall illustrate now, by means of case histories,[41] some of the types of sensorial retinal relationship as they are met with in the examination of patients with concomitant strabismus.

1. NORMAL CORRESPONDENCE IN SPITE OF EARLY ONSET OF STRABISMUS

CASE 3.—E. G., a white girl aged 14 years, came for examination because of considerable eyestrain in close work and in watching moving pictures. Her family history was negative so far as strabismus or other serious ocular defects were concerned. The patient had never been seriously ill. When she was 1½ years of age, it was first noticed that her left eye turned out occasionally, especially when she was tired. This condition had not changed, except for a possible slight improvement during the past few years. At the age of 3 years she was given a pair of glasses; while she wore these glasses the left eye turned out more frequently. The glasses were discarded when the patient was 7 years of age; she had not worn glasses since, nor had there been any other ocular therapy.

Refraction and Visual Acuity.—Right eye: $+1.75$ D. sph. $\frown -0.50$ D. cyl., axis $20 = 20/15 - 1$; left eye: $+2.00$ D. sph. $= 20/20 + 1$.

Retinal Correspondence.—The patient had binocular fixation for distance, but at the slightest provocation (a short and partial covering) the left eye turned out and up; covering the right eye caused this eye to turn out and slightly upward. The cover test revealed a divergent strabismus of 15 arc degrees, with pronounced and variable dissociated vertical divergence.

Double Image Test: There was 15 arc degrees of crossed diplopia with either eye fixating, with 2 to 3 arc degrees of right hypertropia with the red glass in front of the right eye and 8 to 10 arc degrees of left hypertropia with the red glass in front of the left eye (indicating left hypertropia combined with dissociated vertical divergence).

After-Image Test: There was normal localization of positive and negative double images. The near point of convergence was at 10 cm.; convergence was held poorly. However, the patient was able, most of the time, to fixate binocularly at reading distance.

Bar Reading: When fixating binocularly, the patient was able to bar read; when the left eye was in a divergent position, the patient suppressed the images reaching that eye.

Stereoscopic Test: Pictures requiring the second degree of fusion were at times fused; at others the images of the left eye were suppressed; with stereoscopic pictures (Keystone chart DB_6) there was always 100 per cent stereopsis.

Synoptophore: Objectively and subjectively, there were 25Δ of exophoria and 5Δ of left hypertropia; the eyes were always dissociated when first degree

41. These cases were selected, more or less at random, from several hundred cases of concomitant strabismus. They were chosen because they were representative of a certain type of sensorial retinal reaction, not because they were unique. For every type, with the exception of one or two, numerous other examples could be quoted. It is my purpose in the present paper to bring out the typical forms rather than to determine their frequency. The latter will be done in a statistical study of strabismus which is in preparation. Unless it is differently stated, the patients did not show any extraocular or intraocular disease or anomaly except for the strabismus.

pictures were used; there was better cooperation with second degree pictures, and with third degree pictures she always fused, with depth perception.

This instructive case presents the following features. The patient had a divergent strabismus of the left eye and a marked dissociated vertical divergence, indicating that innervational factors played a large part in causing her condition. She was able to overcome the deviation of the left eye both for distance and for near vision, aided in this undoubtedly by her hyperopia. Thus, the strabismus remained latent most of the time, and there was no reason for the development of an anomalous correspondence, which was not found in any of the tests. In fact, the patient had excellent binocular cooperation as long as she kept her divergent strabismus latent, but she needed a strong fusional stimulus to do so. The prognosis in this case is very good. A surgical correction which would remove the necessity for a constant exertion of the convergence, and orthoptic exercises to improve the fusional conditions, should remove completely the subjective symptoms of eyestrain and allow the patient to wear a correction for her hyperopia.

Cases of this type are met with when the patient has a divergent strabismus which he can correct by a convergence impulse, but not all patients show complete absence of anomalous correspondence or such a high degree of binocular cooperation as the patient in case 3.

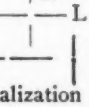
CASE 4.—K. G., a white girl aged 9 years, had a family history without evidence of ocular disorders. When the child was 2 years of age, it was first noticed that her right eye turned out occasionally, especially when she was tired. This condition had remained unchanged since. At the age of 4 years she had orthoptic exercises, which were carried out for two years but were finally discontinued at the suggestion of the physician, who thought them useless. The patient had had no therapy since that time; she had never worn glasses and had no complaint.

Refraction and Visual Acuity.—Right eye = left eye: + 1.25 D. sph. = 20/20.

Retinal Correspondence.—Most of the time there was binocular fixation for distance, but the eyes were easily dissociated in the cover test, which showed divergent strabismus, with an angle of squint of 15 to 17 arc degrees.

Double Image Test: The double images were easily perceived. Their distance varied considerably during the test; most of the time there was a slightly uncrossed diplopia, but at times the patient showed a crossed diplopia of 16 arc degrees. There was no difference in the localization when the fixation changed from the right eye to the left.

After-Image Test: Both the positive and the negative after-images were seen alternately, thus:

and thus: 

, indicating the presence of both normal localization and anomalous localization adapted to the angle of squint.

Stereoscope: The patient had fusion and 100 per cent depth perception with the Keystone DB_6 chart.

Synoptophore: The objective angle was about 25 △ with first degree pictures; it was difficult for the patient to join these pictures; at times she did so at the objective angle, and at others at zero (anomalous correspondence). However, she joined second and third degree pictures with normal correspondence and depth perception at zero, overcoming her strabismus.

Bar Reading: She could bar read and converge fairly well on a pencil.

This case is quite similar to case 3 except for one important factor. The child K. G. also had a divergent strabismus, which she was able to overcome by a convergence impulse; and as long as she kept her strabismus latent her eyes cooperated normally. But all three tests used —the synoptophore test, the double image test and the after-image test —disclosed the presence of an anomalous correspondence with the normal correspondence when the eyes were dissociated. This indicates that the patient's eyes were frequently dissociated and that she had, therefore, acquired a sensorial retinal relationship adapted to this dissociated position.

It is of interest to note that in both case 3 and case 4 the strabismus could be kept latent and that the retinal correspondence was normal when strong fusional stimuli, particularly disparate stimuli, were offered. With first degree pictures in the stereoscope and the synoptophore there was dissociation, and in case 4 anomalous correspondence. Similar observations can be made in certain cases of convergent strabismus.

Case 5.—B. P. B., a white girl 6 years of age, had a negative family history for ocular disorders. Soon after the patient's birth the mother noticed a cast in the right eye. The child had been examined by an ophthalmologist every year since then. Glasses had never been prescribed, but for a while drops (atropine?) were used.

Refraction and Visual Acuity.—Right eye: + 1.50 D. sph. = 20/20; left eye: + 1.75 D. sph. ⌒ × 0.25 D. cyl., axis 85 = 20/30.

Retinal Correspondence.—The cover test showed convergent strabismus of 5 arc degrees in the right eye. The after-image test showed normal correspondence. The double image test revealed both normal and anomalous localization of double images.

Synoptoscope: With first degree pictures, the objective angle was 10△ and the subjective angle 2 △ of esophoria; with second degree pictures normal correspondence was obtained.

In this case of low hyperopia with small convergent deviation and slight amblyopia of the left eye the anomalous correspondence was again only superficially established; this is apparent from the fact that the localization of the after-images was always normal and that both normal and anomalous correspondence were evident in the double image test and in the test with the synoptoscope. The feature of the case which I wish particularly to stress is the appearance of normal correspondence when strong fusional stimuli were exerted (second degree pictures in the synoptoscope), while the correspondence was anomalous when there

were no, or only weak, fusional stimuli (first degree pictures in the synoptoscope). This finding, aside from being of prognostic value as to the result of orthoptic exercises, indicated that the patient could and did use her eyes together when the conditions were favorable. It must not be construed as being in contradiction to the thesis, set forth in the discussion of the tests for retinal correspondence, that one is more likely to elicit anomalous correspondence the closer the conditions of the test approximate the normal conditions of seeing. In this case the eyes were frequently used properly in normal environments. Only when the conditions for fusion were poor (either because no fusional stimuli were present in the field of view or because the child was tired) did the eyes dissociate; but this had happened frequently enough to permit the development of anomalous correspondence.

The reason that the children in cases, 3, 4 and 5 showed normal correspondence in spite of an early onset of strabismus is to be found in the ability of all 3 patients to keep their eyes straight and use them together a good deal of the time. There is a second group of patients who persist in localizing according to the innate normal correspondence, but who do so for exactly the opposite reason. These patients retain the normal correspondence because they have never kept their eyes straight and have never used them together, so that there has arisen no opportunity for the development of anomalous correspondence.

Case 6.—E. R., a white girl, was 8 years old when she was first seen. A paternal aunt had strabismus; the family history was otherwise negative for ocular difficulty. It was first noticed when the child was 18 months of age that the right eye was turning in; this occurred after a sickness from whooping cough and measles. She had worn glasses since the age of 3 years but had had no other treatment.

Refraction and Visual Acuity.—Right eye: $+5.00$ D. sph. $\bigcirc +1.00$ D. cyl., axis $90 = 20/100 - 1$; left eye: $+5.00$ D. sph. $= 20/20$.

Retinal Correspondence.—In the cover test, with correction there was a convergent strabismus of the right eye of 25 arc degrees, covered to a large extent by a negative angle gamma. The double image test and the after-image test showed normal correspondence.

A tenotomy of the right internal rectus muscle reduced the angle of squint to 9 arc degrees; owing to the large angle gamma, the eyes appeared parallel for distance. Two years later the double image and after-image tests still showed normal correspondence.

In this case of high hyperopia, high amblyopia and unilateral strabismus of large amount, one is justified in assuming that the binocular cooperation never developed beyond the stage of innate common visual directions and that the patient never used her eyes together sufficiently to establish anomalous correspondence. But a similar behavior can also be observed in cases of alternating strabismus in which the visual acuity is equal in the two eyes and in which the angle of squint—at least with correction—is not very large.

CASE 7.—B. P., a white girl, was 5 years of age when first seen; she had been observed over a period of four years. Her mother was highly far sighted and had intermittent convergent strabismus; several members of the family on the maternal side were highly far sighted. It had been noticed since the patient's birth that either eye turned in intermittently; she had had no previous ocular examination or treatment.

Refraction and Visual Acuity.—Right eye: +5.00 D. sph. ⌒ +2.00 D. cyl., axis 75 = 20/25; left eye: +5.00 D. sph. ⌒ +2.00 D. cyl., axis 90 = 20/25.

Retinal Correspondence.—In the cover test there was alternating convergent strabismus of 35 to 40 arc degrees without glasses and of 15 to 16 arc degrees with glasses, with some left hypertropia. Because of a large angle gamma, the eyes appeared straight with glasses. The patient could fixate with either eye and alternated to some extent at will but preferred the right eye for fixation. There was a slight excess of adduction in each eye, being greater in the left eye, with pronounced overfunction of the left inferior oblique muscle.

Synoptophore: The objective angle of squint was 34△, with 2½△ of left hypertropia, and a subjective angle of 2 to 4△.

Double Image Test: At times there was no horizontal displacement of the double images; at others there was 15 arc degrees of uncrossed diplopia with either eye fixating.

After-Image Test: Positive and negative after-images were always normally localized.

Stereoscopic Examination: There was always strictly uniocular vision.

This patient came from a highly hyperopic family on the maternal side. She herself had a typical accommodative strabismus with equal visual acuity of the two eyes. The strabismus, noticeable since her birth, had always been alternating. She had apparently used her eyes together only infrequently, and there was therefore no reason for her to acquire a deeply rooted anomalous correspondence. She showed, accordingly, always a normal localization of the after-images. There was, however, at times an anomalous correspondence adapted to the angle of squint in the synoptophore and in the double image test, which is proof of the existence of occasional cooperation of her two eyes. But this cooperation was not of sufficient duration or frequency to cause a complete repression of the normal retinal relationship.

Cases 6 and 7 are particularly significant in a theoretic respect. They can be interpreted only on the basis of the nativistic theory. If the common visual directions were acquired by proper use of the eyes, then a child who has had a strabismus ever since birth could not show a normal retinal relationship; the commonness of the visual directions must have existed prior to and independent of the use of the eyes; in other words, it is innate.

2. ANOMALOUS CORRESPONDENCE ADAPTED TO THE ANGLE OF SQUINT

CASE 8.—J. M., a white girl 16 years of age, had one cross-eyed cousin. Otherwise there was no strabismus in the family. When the patient was 2 years of age, an alternating convergent strabismus developed, following whooping cough.

She had worn glasses since the age of 4 years and had had prism fit-overs (both eyes, 6△ base out) for one year. She had had no other therapy. Between the ages of 6 to 8 years she had occasional spontaneous diplopia, but never since.

Refraction and Visual Acuity.—Right eye: +1.75 D. sph. = 20/20; left eye: +1.75 D. sph. = 20/15.

Retinal Correspondence.—Cover Test: With refractive correction, there was 12 to 15 arc degrees of alternating convergent strabismus for distance and near vision; the left eye was preferred for fixation.

Double Image Test: With the refractive correction alone there was an uncrossed diplopia of 6 arc degrees with either eye fixating; with refractive correction and prism fit-overs there was no horizontal displacement of the double images, although the cover test still showed 6 arc degrees of alternating convergent strabismus. After-Image Test: The after-images were normally localized.

Stereoscope: Most of the time there was alternating uniocular vision; at times there was fusion of second degree pictures, but there was no stereopsis.

In this case the normal correspondence was no longer as prevalent as in the preceding cases. The patient's response to the after-image test was normal, to be sure; but the double image test showed a well established anomalous correspondence, and the angle of anomaly was, interestingly enough, adapted to the peculiar circumstances of the case. With her refractive correction, the patient had objectively 12 arc degrees of convergent strabismus, and in the double image test, an angle of anomaly of 6 arc degrees. This angle of anomaly corresponded exactly to the residual angle of squint when the prism fit-overs were worn. In other words, the patient had acquired an angle of anomaly which exactly offset the deviation to which she had become accustomed by wearing the prism fit-overs constantly for about one year.

Such an adaptation to the particular circumstances of the case is often well demonstrated in cases of accommodative strabismus when the patient's sensorial reaction is tested with and without his glasses.

Case 9.—M. S., a white boy, was 3 years of age when first seen. Both his father and his mother had an amblyopic eye. One year prior to the examination the boy had whooping cough, after which an occasional turning of the left eye was observed. The patient had not been treated previously for his ocular condition.

Refraction and Visual Acuity.—Right eye: +5.00 D. sph. = 20/20—; left eye: +5.00 D. sph. = 20/70.

Retinal Correspondence.—The patient wore these glasses constantly for three years. At the end of this period the following condition was found: Cover test: Without correction there was 22 arc degrees of convergent strabismus in the left eye; with correction the angle of squint was reduced to 10 arc degrees.

Double Image Test: With correction double images coincided; without correction there was an uncrossed diplopia of 10 arc degrees.

After-Image Test: Positive and negative after-images showed a horizontal separation of 10 arc degrees, irrespective of whether or not glasses were worn.

Synoptophore: Objectively, there was 10 arc degrees of esotropia with correction and 24 arc degrees without correction: subjectively, with correction the angle was zero, and without correction there was 12 arc degrees of esotropia with first degree pictures.

The retinal correspondence in this case was harmoniously adapted to the angle of squint existing when the patient wore his correction. When the retinal correspondence was tested with the synoptophore and in the double image test, a harmonious anomalous correspondence was found when the patient wore his glasses; the anomalous retinal correspondence was unharmonious in these tests when the patient did not have his glasses on. The result of the after-image test was, of course, not influenced by the glasses.

In this case the retinal correspondence was fully adapted to the patient's habitual angle of squint. The situation was similar in the next case.

CASE 10.—A. MacD., a white girl 9 years old, had a negative family history for ocular disorders. It had been noticed since she was born that her right eye turned in. She had worn glasses since the age of 4 years but otherwise had had no therapy.

Refraction and Visual Acuity.—Right eye: + 3.00 D. sph. ⌒ + 0.50 D. cyl., axis 90 = 20/30—2; left eye: + 3.00 D. sph. + 0.50 D. cyl., axis 90 = 20/20.

Retinal Correspondence.—Cover Test: There were 6 arc degrees of convergent strabismus in the right eye.

Double Image Test: The double images coincided and followed the prism displacement in all directions.

After-Image Test: The positive and negative after-images were seen thus:

| R
——— —— L
|

The interpretation of this case is simple. The patient had a unilateral convergent strabismus of long standing and small amount. For a number of years she had worn an adequate correction for her hyperopia. Her neuromuscular condition had been balanced for a number of years, and she had acquired a well established anomalous correspondence; both the double and the after-image test showed a localization adapted to the angle of squint.

The fact that such cases exist and are, indeed, rather frequent is one of the most important arguments in favor of the concept of anomalous correspondence adopted in this paper.

If this concept is correct, there ought to be an adaptation of the visual directions not only in the horizontal but also in the vertical sense. Such an occurrence can occasionally be observed, particularly if the vertical deviation is large.

CASE 11.—M. W. R., a white youth aged 18, a high school student, had a maternal uncle who was cross eyed. The patient himself had been cross eyed since the age of 2½ years, when he fell downstairs, after which his right arm was paralyzed for a while.

Refraction and Visual Acuity.—Right eye: + 3.00 D. sph. ⌒ — 2.50 D. cyl., axis 10 = 20/20; left eye: + 3.00 D. sph. ⌒ — 3.00 D. cyl., axis 170 = 20/20.

Retinal Correspondence.—The patient fixated most of the time with the right eye but was able to alternate the fixating eye at will. There was an alternating

convergent strabismus of approximately 40 arc degrees, with approximately 6 arc degrees of left hypertropia and a dissociated vertical divergence. The adduction was extremely excessive, particularly in the right eye. The abduction was deficient. The case was complicated by other deficiencies and overactions in the excursions of the eyeballs which are not pertinent to the present discussion.

Double Image Test: There was either no horizontal deviation or an uncrossed diplopia of 10 to 14 arc degrees when fixating with either eye; a dissociated vertical divergence of up to 3 or 4 arc degrees became manifest after covering either eye for a few seconds with the red glass.

After-Image Test: The horizontal after-image (both positive and negative) was separated by a very large distance from the vertical after-image (35 to 40 arc degrees) and was higher when produced in the left eye and lower when produced in the right eye (vertical distance approximately 6 arc degrees). The patient was operated on, with good cosmetic result in so far as the horizontal deviation was concerned. The after-image test, taken at frequent intervals, had yielded the same result over a period of nearly two years.

In this patient, a sensorial adaptation to the motor condition had taken place not only in the horizontal but also in the vertical direction: In the double image test there was no vertical displacement of the double images (except for the concurrent dissociated vertical divergence), and in the after-image test there was a vertical separation of the after-images, which corresponded to the patient's left hypertropia.

However, as was pointed out, the adaptation of the sensorial retinal relationship to changed mechanical conditions is a process requiring time. It would not be reasonable to expect it to be accomplished at all levels at the same time. One therefore finds quite often that the angle of anomaly is not adapted to the angle of squint, either in one or in all of the tests. There is always a reason for this (for instance, a recent operation which has changed the position of the eyes), which may or may not be known.

3. ANOMALOUS CORRESPONDENCE PARTIALLY ADAPTED TO THE ANGLE OF SQUINT

CASE 12.—G. H., a 13 year old girl, was the daughter of irresponsible parents and was herself of a mental age considerably below her chronologic age. No ocular history was available. The child complained of eyestrain.

Refraction and Visual Acuity.—Right eye: +2.00 D. sph. = 20/20; left eye: +2.50 D. sph. = 20/70.

Retinal Correspondence.—Cover Test: The left eye showed convergent strabismus of 5 to 6 arc degrees. The patient was able to fixate with the left eye.

Double Image Test: Repeated tests showed that the double images coincided and followed exactly the prism displacement in all directions.

After-Image Test: The negative after-images were seen thus (a positive after-image could not be obtained): R—— ——
|L
|

This case is reported because of the difference in the results of the double image and the after-image test. In the double image test the

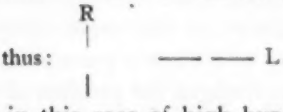
angle of anomaly was 5 to 6 arc degrees; in the after-image test, 15 to 16 arc degrees. This can be interpreted only as meaning that the angle of squint had been larger at some time before than it was at the time of the examination, and that the sensorial condition was not as yet fully adapted to the changed motor conditions. Such an adaptation had taken place as far as the ordinary conditions of seeing were concerned, which were approximated in the double image test. But as soon as the patient was given an unusual visual problem, such as is provided in the after-image test, a former mode of localization was resorted to.

It is not known why the angle of squint had changed in this case, but in other cases it is known that the change was caused by an operative procedure. The history of a case belonging to this group is reported next.

CASE 13.—A. M., an Italian aged 43, came for examination because he felt the need of a change in his glasses. The family history was negative for strabismus. The patient's right eye began to turn in when he was 2 years of age, after a severe infectious disease, possibly encephalitis. At the age of 27 he was operated on for his strabismus.

Refraction and Visual Acuity.—Right eye: $+4.00$ D. sph. $\frown +1.00$ D. cyl., axis $90 = 20/400$; left eye: $+3.00$ D. sph. $\frown +1.25$ D. cyl., axis $90 = 20/20$.

Retinal Correspondence.—For distance there was a convergent strabismus of the right eye; the movement was offset in the cover test by a prism of 15△. The rotations of both eyes were normal. The double image test showed uncrossed diplopia of 2 arc degrees when the left eye fixated and crossed diplopia of 2 arc degrees when the right eye fixated. In the after-image test, the positive and negative after-images were seen thus:



It is quite apparent that in this case of high hyperopic astigmatism and amblyopia ex anopsia of the right eye the double image test was roughly adapted to the present small angle of squint, while the after-image test showed an anomalous relationship adapted to the preoperative angle of about 30 to 35 arc degrees. It is of interest to note that this anomalous relationship still existed, although the operative change in the position of the eyes had occurred sixteen years prior to the examination.

That the interpretation given to the findings in this case is correct is shown by a case which I have followed over a period of six years.

CASE 14.—M. W., a white school girl, was 16 years of age when first seen. She had a negative family history for ocular disease. Her left eye had turned in since birth. She had worn glasses since the age of 6 years; for a time the right eye was occluded.

Refraction and Visual Acuity.—Right eye: $+1.00$ D. sph. $\frown +2.25$ D. cyl., axis $75 = 20/20$; left eye: $+1.00$ D. sph. $\frown +2.25$ D. cyl., axis $105 = 20/25-2$.

Retinal Correspondence.—The cover test showed convergent strabismus of the left eye of 20 arc degrees. There were an excess of adduction, particularly in

the left eye; an overfunction of the inferior oblique muscles, and a pronounced dissociated vertical divergence. The double image test showed anomalous correspondence adapted to the angle of squint. The positive and negative after-images were seen thus: R —— —— | L |

A tenotomy of the left internal rectus was performed, which reduced the angle of squint to 8 or 10 arc degrees. After the operation the double image test showed crossed diplopia of 8 arc degrees; the after-image test showed no change. Two years after the operation the localization of the double images was adapted to the angle of squint; the after-images were still localized in the same way as before the operation. Six years after the operation, when the patient was seen last, refraction and visual acuity were essentially unchanged. The cover test showed a residue of convergence of 8 arc degrees, covered by a large angle gamma. There was a deficiency of adduction in the right eye; the condition of the motility was otherwise unchanged. The double image test showed at times only vertical displacement of double images according to the vertical divergence and at others 2 arc degrees of uncrossed diplopia. The localization of the after-images was the same as before the operation.

The history of this patient demonstrates that in cases of deeply rooted anomalous correspondence the after-images may be localized in an anomalous way adapted to the preoperative angle of squint even many years after the operation. Only a partial adaptation to the postoperative mechanical conditions had taken place in this case, as was evidenced by the double image test, but the adaptation was too superficial to have caused a change in the localization of the after-images. This explains the difference between the results of the double image and the after-image test.

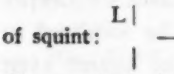
4. CHANGE IN SENSORIAL REACTION WITH DISSOCIATION OF THE EYES

In cases 4 and 5, in which both normal and anomalous correspondence were present, a careful observation of the patient's eyes during the tests showed that the change in localization was not accomplished by a change in the position of the patient's eyes. In certain rare instances, however, it can be demonstrated even in the after-image test that the position of the patient's eyes (i. e., whether or not the eyes are dissociated) influences the type of localization used by the patient. The results obtained in these cases, which were mentioned in the discussion of the after-image test, might easily be misconstrued, and I therefore cite an instructive case belonging to this group.

CASE 15.—F. P. C., a white man aged 32, with a negative family history for ocular disorders, complained of photophobia, ocular fatigue and severe headaches after using his eyes. It had been noticed since he was 3 years of age that either eye turned out, and ever since he could remember he had had the ability to let either eye turn out at will. The patient had always had good health, but he claimed to be highly nervous; in fact, a few years previous to the examination he had a severe nervous breakdown and had to be confined to an institution.

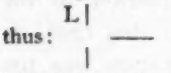
Refraction and Visual Acuity.—Right eye = left eye: +0.25 cyl., axis 90 = 20/15.

Retinal Correspondence.—The eyes were parallel for distance, but the cover test showed an alternating divergent strabismus of 25 arc degrees. The patient could control his eyes perfectly; he could either keep them straight or let either eye diverge at will. He converged perfectly on a pencil, and the convergence was well held. In the double image test, when the red glass was placed in front of either eye for a very short while, the double images coincided; but when the red glass was kept long enough in front of one eye so that the eyes were dissociated, the localization of the double images became extremely uncertain. The patient reported most of the time that he saw two entirely separate images which had no relation to each other, although he saw them simultaneously. This behavior was checked with the projection instrument, in which the two eyes are dissociated by means of polaroid material.[14] When a dot was presented to one eye and a tangent scale to the other eye, the patient was again unable to localize the dot in relation to the scale; but when a binocularly seen square of light was projected at the same time on the screen, the patient fused the square and localized the dot properly in relation to the tangent scale. The results obtained with the after-image test were particularly interesting. The positive after-images were always localized according to anomalous correspondence adapted to the angle of squint:

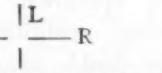


The negative after-images were localized either

thus:



or thus:



The first mode of localization occurred when the patient dissociated his eyes; the second, when he kept them straight (which he could do in the lighted room, but not in the dark). With the stereoscope, as well as for distance with the projection instrument, the patient had 100 per cent depth perception with the DB$_6$ Keystone chart.

There was a pronounced deficiency of adduction in both eyes, and advancement with resection of both internal rectus muscles was performed. One month after the operation, there was a residue of divergence of 5 arc degrees in the cover test; the patient was no longer able to dissociate his eyes at will. In the double image test there was an uncrossed diplopia of 20 to 22 arc degrees (anomalous correspondence adapted to the preoperative angle of squint), and there was now no difficulty in localizing the double images. As before the operation, the double images coincided when the red glass was placed only for a short while in front of one eye. The positive after-images were now localized most of the time normally; occasionally there was a displacement of the vertical after-image of the same amount as prior to the operation. The negative after-images always formed a cross; in none of the numerous tests were they localized anomalously.

The salient features of this highly interesting case can be summarized as follows: The patient had a facultative divergent strabismus of 25 arc degrees. When he kept his eyes straight, he had normal binocular vision. When his eyes were dissociated, he showed anomalous correspondence in the double image test. Before he was operated on, he had great difficulty in localizing the double images, but it can be assumed that his anomalous sensorial reaction in this test was adapted to the angle

of squint, since he showed a crossed diplopia of 20 arc degrees after the operation, which had reduced his angle of divergent strabismus from 25 to 5 arc degrees. After the operation he had no difficulty in localizing the double images. The after-image test showed a peculiar behavior. The positive after-images (seen by the patient in the dark) always presented a displacement adapted to the angle of squint; the negative after-images either formed a cross or were displaced by the amount of the angle of squint, according to whether or not the eyes were dissociated. The fact that the patient was unable to keep his eyes straight in the completely darkened room explains why the positive after-images never appeared as a cross. After the operation the behavior of the after-images changed to some extent. The patient was now unable to dissociate his eyes at will, and the negative after-images were always localized normally. This mode of localization prevailed even in the dark; only occasionally was there a recurrence of the old mode of localization.

It must be emphasized once more that even in this case the position of the after-images did not change because of the change in the direction of the line of gaze of one eye when the eyes were dissociated. The change in the position of the after-images was caused by a change in the sensorial retinal relationship, which in this particular instance was dependent on whether or not the eyes were used together.

The difference in the localization of the positive and the negative after-images shown by this patient is typical for cases with facultative divergent strabismus. A number of instances could be cited to corroborate this statement, but I shall restrict myself to referring to a case history which I have recently published.[42]

If the explanation given here for the phenomenon is correct, the phenomenon should not occur in patients who are unable to control the position of their eyes. I do not recall any instance in which it did. However, at times even such patients show differences in the localization of the after-images, as will be seen in the next case.

CASE 16.—T. M. C., a white girl aged 9 years, had a negative family history for strabismus. Only when she was 4 years of age, after a fall downstairs, was it noticed that her left eye began to turn in.

Refraction and Visual Acuity.—Right eye: + 5.00 D. sph. ⌒ + 0.50 D. cyl., axis 90 = 20/20; left eye: + 4.00 D. sph. ⌒ + 2.50 D. cyl., axis 110 = 20/40 + 3.

Correspondence.—With this correction there was a convergent strabismus of the left eye of 20 arc degrees. The patient fixated habitually with the right eye but was able to fixate with the left eye.

Double Image Test: Most of the time there was 20 arc degrees of uncrossed diplopia with either eye fixating; occasionally there was no horizontal deviation of the double images, but this occurred only when the right eye fixated.

42. Burian, H. M.: A Visual Phenomenon Related to Binocular Triplopia, Am. J. Ophth. **26**:1084, 1943.

After-Image Test: The positive after-images were always localized according to normal correspondence; the negative ones were localized almost always according to anomalous correspondence adapted to the angle of squint.

The behavior of this patient in the after-image test was the reverse of the behavior shown by patients with facultative divergent strabismus: In the darkened room there was normal correspondence; in the lighted room the correspondence was anomalous. The reason for this is that the conditions of seeing in the darkened room were unusual for the patient. Her anomalous correspondence was not deeply rooted, as was evidenced also by the double image test, and she reverted immediately to the normal mode of localization when placed under an unusual condition.

There is no contradiction in the response of the after-image test in the two types of cases discussed in this section. In fact, the findings supplement and corroborate each other.

5. CHANGE IN SENSORIAL REACTION WITH CHANGE IN FIXATION AND WITH SELECTIVE STIMULATION OF VARIOUS RETINAL AREAS

Changes in the sensorial reaction occur not only depending on whether or not the eyes of the patient are dissociated; they may also occur when fixation is changed from one eye to the other.[43] This difference in reaction is, again, not due to the change in the actual position of the eyes.

Case 17.—J. C. W. was a white girl aged 7 years whose father had strabismus. It was noticed when she was 2½ years of age that her left eye turned in, the convergence being greater when she was tired. She had worn glasses for some time but had had no other therapy.

Refraction and Visual Acuity.—Right eye: + 1.50 D. sph. ⌒ + 1.50 D. cyl., axis 70 = 20/20; left eye: + 0.75 D. sph. ⌒ + 2.75 D. cyl., axis 90 = 20/30.

Retinal Correspondence.—Cover Test: There was 8 arc degrees of convergent strabismus of the left eye.

Double Image Test: When the right eye fixated, the double images were slightly crossed or slightly uncrossed (anomalous correspondence); when the left eye fixated, there was an uncrossed diplopia of 8 arc degrees (normal correspondence).

After-Image Test: The after-images were localized according to normal correspondence.

This patient had normal correspondence in the after-image test. In the double image test she showed anomalous correspondence when she fixated with her right eye. But when she was forced to fixate with

43. The first to observe such behavior was A. von Graefe, in 1855.[19] His patient showed a small residue of convergent strabismus of the left eye after operation. When the patient fixated with the right eye, there was always a crossed diplopia with considerable distance of the double images (anomalous correspondence). When he fixated with the usually deviated left eye, there was an uncrossed diplopia of small amount (normal correspondence).

her left eye, which was usually deviated, she used her eyes under conditions to which she was not accustomed and she localized immediately in the normal way. In this patient the anomalous correspondence was not deeply rooted, but the same behavior can be observed in patients in whom the anomalous correspondence has gained a much stronger hold.

CASE 18—J. B., a white girl aged 12, had been under my observation since she was 6½ years of age. She had a maternal uncle with strabismus; turning of her right eye was first noticed when she was 4 years of age.

Refraction and Visual Acuity.—Right eye: $+3.00$ D. sph. $\bigcirc +2.00$ D. cyl., axis $90 = 20/20 + 1$; left eye: $+2.75$ D. sph. $\bigcirc +1.00$ D. cyl., axis $100 = 20/20$.

Retinal Correspondence.—Cover Test: There was 5 to 6 arc degrees of convergent strabismus of the right eye.

Double Image Test: There were crossed diplopia of 8 to 10 arc degrees when the left eye fixated (anomalous correspondence) and uncrossed diplopia of 5 arc degrees when the right eye fixated (normal correspondence).

After-Image Test: Positive and negative after-images showed anomalous correspondence angle of anomaly 15 arc degrees): R — — L

On two occasions the positive after-images were localized thus:

R — — L (angle of anomaly 5 to 6 arc degrees).

Synoptophore: There was an objective angle of 10 to 12△ of esophoria and a subjective angle of zero.

In this case there was, again, a difference in the mode of localization of the double images, depending on whether the patient fixated with the habitually deviated eye or with the eye that habitually fixated. Again, the correspondence was normal when the patient fixated with the eye which was as a rule turned.

The case is especially interesting because the patient presented two types of anomalous localization. In the synoptophore test the angle of anomaly was equal to the angle of squint; in other words, in this test, which most closely approximates the habitual conditions of seeing, the anomalous correspondence was adapted to the anomalous motor condition revealed by the cover test. In the double image test as well as in the after-image test, the angle of anomaly was larger than the angle of squint, indicating again that the angle of squint must have been larger in times past. One encounters such a situation relatively frequently in the after-image test, but it is unusual to find it also in the double image test, except shortly after an operation.

A change in the mode of localization takes place not only when the leading eye gives up fixation and the deviated eye assumes it, but also when certain artificial conditions of biretinal stimulation are created which differ from those to which the eyes of a squinting patient are habitually exposed.

When a squinting patient fixates a certain object, say, the light of the Maddox cross, the image of that object falls on the fovea of the fixating eye and on an eccentric element of the retina of the other eye. The patient may then show an anomalous localization of the double images. If the arrangements of the test are now changed in such a way that the image of the object is formed on the fovea in both eyes, unusual conditions of bifoveal stimulation are created for which the patient is not adapted. It may then happen, and I have observed this frequently, that the patient suddenly localizes the double images according to normal correspondence. I have described such cases in an earlier publication,[15] and I mention them here in further support of the thesis that in many cases in which the anomalous correspondence is not too deeply rooted it depends on the conditions under which the tests are performed whether a normal or an anomalous sensorial response of the patient will be elicited.

6. POSTOPERATIVE CHANGES IN THE MODE OF SENSORIAL REACTION

The spontaneous changes in the sensorial relationship following an operative change in the position of the eyes offer an excellent means of studying the adaptation of the sensorial reaction to the changed motor conditions.

Both Bielschowsky [31] and, particularly, Ohm [44] have paid attention to the postoperative development of the retinal correspondence and have stated that squinting patients go through three stages after successful surgical treatment. In the first stage the correspondence is anomalous; in the second there is a rivalry between normal and anomalous correspondence and in the third the normal correspondence is reestablished.

A development such as that postulated by Ohm would, indeed, seem to be the natural course which one would expect squinting patients to follow whose eyes had been straightened by a surgical procedure. Actually, however, as Ohm himself pointed out, only few patients go through all three stages. The spontaneous development toward normalcy may stop at any stage. The factors on which this development depends are similar to those which influence the preoperative establishment of anomalous correspondence. These factors are: (1) the age of the patient at the time of the operation; (2) his individual adaptability; (3) the thoroughness with which the anomalous correspondence was established at the time of the operation, and (4) the use the patient makes of his eyes after the operation.

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44. Ohm, J.: Klinische Untersuchungen über das Verhalten der anomalen Sehrichtungsgemeinschaft der Netzhäute nach der Schieloperation, Arch. f. Ophth. **57**:439, 1908.

After operation, in rare instances the patient spontaneously regains not only normal correspondence but also normal binocular vision. Much more frequently one finds that either the normal sensorial reaction is now the rule (but that normal binocular vision has not developed) or normal and anomalous localization are alternately present. The majority of the patients do not even reach this second stage of Ohm's spontaneously, but the reaction stabilizes itself in an anomalous sensorial relationship adapted to the new motor conditions; or the patients may even retain, at least in the after-image test, the anomalous correspondence acquired previous to the operation.

Two cases of the latter type have already been discussed (cases 13 and 14). In both instances the patients were relatively old at the time of the operation (16 and 27 years, respectively). They adapted themselves in a superficial way to the new motor conditions created by the operation (anomalous correspondence adapted to the angle of squint in the double image test), but their deeply rooted anomalous correspondence acquired prior to the operation still manifested itself in the after-image test years after the surgical procedure was performed.

The behavior of a small child whom I had under my care was very different in this respect.

CASE 19.—M. M., a white girl, was 3½ years old when first seen. She had a negative family history for strabismus. It was first noticed one year previous to the examination that the left eye turned in, after the child had had an abscess of the left ear. She received glasses at that time.

Refraction and Visual Acuity.—Right eye: + 5.00 D. sph. = 20/20; left eye: + 5.00 D. sph. ⊃ + 0.50 D. cyl., axis 90 = 20/20 — 2.

Retinal Correspondence.—The cover test showed 20 to 25 arc degrees of convergence in the left eye. There was a marked excess of adduction in both eyes, with some overaction of the right inferior oblique muscle. The double image test showed no horizontal displacement of the double images and 1 to 2 arc degrees of right hypertropia; the double images followed the prism displacement in all directions. The after-image test was attempted but the result was uncertain. Two years later the condition was unchanged in all respects. A tenotomy of the left internal rectus was performed. The left eye was covered for only two days. Seven days after the operation there was a residue of convergence of 15 arc degrees. Even at that time the double image test again showed no horizontal, but only a vertical, displacement of the double images. Two months after the operation, the residue of convergence was 7 arc degrees, the double image test showed no horizontal displacement and the after-image test presented an anomalous correspondence adapted to the angle of squint (positive and negative after-images): R $\frac{|}{——}$ $\frac{L}{——}$ |

It is possible that the rapid adaptation of the sensorial to the motor conditions in this case was due to the youth of the patient. It is not accidental; I have seen it happen in a number of instances.

In the second postoperative stage there exists a rivalry between normal and anomalous localization. The normal correspondence is reawakened, but the anomalous correspondence is still present. As a result, two directional localizations were alternately attributed to the foveal stimulations. As a rule, these two directional localizations are present only successively. The foveal stimulus is localized now in a normal, now in an anomalous, way. In certain cases, however, the normal and anomalous localizations are present simultaneously, and the stimulus is then localized in two different directions at the same time. This striking feature is known as monocular diplopia, or binocular triplopia. It is not frequently met with and can often be demonstrated only for a fleeting moment. In other cases it is present more or less constantly and can be observed in the same patient over a number of years.

CASE 20.—B. B., a 13 year old white girl, had one cross-eyed cousin. When the patient was 9 months of age, it was first noticed that her left eye was turning in. She had worn glasses for about seven years.

Refraction and Visual Acuity.—Right eye: $+0.25$ D. sph. $\bigcirc$ $+0.50$ D. cyl., axis $90 = 20/15$; left eye: $+3.00$ D. sph. $\bigcirc$ -0.50 D. cyl., axis $55 = 20/20$.

Correspondence.—The cover test showed 20 to 25 arc degrees of convergent strabismus. The patient was able to fixate with the left eye but fixated habitually with the right eye. There were a very large excess of adduction in each eye, a slight overaction of the inferior oblique muscle of the left eye and a dissociated vertical divergence. The results of the double image test were not recorded at the first examination. The after-image test showed anomalous correspondence. A guarded tenotomy of the left internal rectus muscle was performed; the bandage was removed on the second day. On the fourth postoperative day, before being discharged, the patient showed a residue of convergence of 8 to 10 arc degrees in the cover test. The double image test revealed both crossed diplopia of 12 to 14 arc degrees and uncrossed diplopia of 4 to 5 arc degrees, present most of the time successively, and at times binocular triplopia. One month after the operation the angle of squint was again 15 arc degrees. The double image test showed an uncrossed diplopia of about 15 arc degrees with the left eye fixating. With fixation of the right eye localization of the double images was uncertain, but there was always crossed diplopia of about 3 to 4 arc degrees. A guarded tenotomy of the right internal rectus muscle was done, which reduced the angle of squint to 5 arc degrees. On the fourth postoperative day, the double image test showed alternately 20 arc degrees of crossed and 5 arc degrees of uncrossed diplopia; these two types of localization were present either alternately or simultaneously (binocular triplopia). In a later examination the binocular triplopia was never again observed, although the rivalry between normal and anomalous localization continued to exist. Six months after the first tenotomy a myectomy of the left inferior oblique muscle was performed, which completely removed the overaction of that muscle. At that time the crossed and uncrossed diplopia were still both present in the double image test and the after-image test showed both normal and anomalous correspondence. In the course of time the localization of the double images in the double image test tended to become adapted to the angle of squint; the after-image test always showed normal

correspondence. The patient was last seen two and a half years after the first operation. She then showed 1 arc degree of crossed diplopia when fixating with the right eye and 2 arc degrees of uncrossed diplopia when fixating with the left eye.

In some exceptional cases the patient regains spontaneously full binocular vision after an operative correction of the position of his eyes, in spite of an early onset of the strabismus and the existence of anomalous correspondence prior to the operation. The following case illustrates this all too rare type. At the same time, it offers an example of the cases in which all three stages postulated by Ohm [44] are successively represented.

CASE 21.—F. S. L., a 10 year old white boy with a negative family history for ocular disorders, had had a convergent strabismus since the age of 3 years, after a fall downstairs. He had worn glasses since the age of 5 years.

Refraction and Visual Acuity.—Right eye: + 2.75 D. sph. = 20/15; left eye: + 2.50 D. sph. = 20/15.

Retinal Correspondence.—The cover test showed an alternating convergent strabismus of 24 arc degrees, but the left eye was habitually used for fixation. There were a high bilateral excess of adduction and an overaction of the right inferior oblique muscle. The double image test showed anomalous correspondence adapted to the angle of squint; the after-image test revealed both normal and anomalous correspondence. Guarded tenotomies of the right and left internal rectus muscles, performed within one month, reduced the angle of squint to 2 arc degrees. For a short time after the operations there was crossed diplopia in the double image test, which soon disappeared. Five months after the operation there was no movement in the cover test; the double image test showed ½ to 1 arc degree of uncrossed diplopia, and the after-image test was normal. In the stereoscope there was alternating uniocular vision. Eight months after the operation the results of the cover test, the double image test and the after-image test were unchanged, but in the stereoscope there were fusion and 100 per cent depth perception with the graduated Keystone DB_6 and the Bausch and Lomb cards. However, the bar reading test indicated absence of binocular vision. The condition was the same when the patient was last seen, thirteen months after the operation.

7. BINOCULAR COOPERATION IN ANOMALOUS CORRESPONDENCE

If anomalous correspondence is an attempt to restore binocular vision on the basis of an abnormal motor condition, then the question must be asked: How successful is this attempt? In other words, is there a binocular visual act in patients with concomitant strabismus and anomalous correspondence comparable to that of normal persons?

The answer is: There can be, indeed, a high degree of binocular cooperation with anomalous correspondence. It has been shown by other investigators, and in many of the sample cases reported in this paper, that the anomalous correspondence is frequently well adapted to the angle of squint. Thus, the basic prerequisite for binocular vision, the commonness of the visual directions of simultaneously stimulated

retinal elements, is fulfilled. There is undoubtedly simultaneous perception with anomalous correspondence, and Bielschowsky [31a] has demonstrated that binocular color mixture may exist in such cases. I was able to prove that there may even be fusional movements with anomalous corresponding retinal areas,[15] but the highest degree of binocular cooperation, stereopsis, is never achieved.

Again, it must be kept in mind, in studying the binocular visual act in anomalous correspondence, that anomalous retinal correspondence may be more or less well established. If it is present only occasionally and under special conditions, it cannot be expected to afford as complete a binocular cooperation as when it is deeply rooted and established more or less permanently. In the latter condition, however, it may lead to a surprisingly high cooperation between the two eyes. This can be seen from the following case, which concludes this survey of the clinical picture of anomalous correspondence.

CASE 22.—M. H., a white girl aged 9 years, had a negative family history for strabismus. Alternate turning in of the eyes was first noticed when the patient was 2 years old.

Refraction and Visual Acuity.—Right eye: +6.00 D. sph. ⌒ −1.00 D. cyl., axis 180 = 20/20; left eye: +7.00 D. sph. ⌒ −2.00 D. cyl., axis 180 = 20/20 −2.

Correspondence.—The patient was observed over a period of four years, and the behavior of her eyes always remained the same. With correction there was an alternating convergent strabismus of 10 arc degrees. The double image test and the after-image test showed anomalous correspondence adapted to the angle of squint. The eyes responded to vertical disparity introduced by prisms (fusional movements present with central stimulation). In the stereoscope there was superimposition of images but alternate suppression of disparate stimuli (grade II binocular vision; no stereopsis). With the projection instrument [15] fusional movements could be elicited when the targets were superimposed on the screen (anomalous correspondence). When the targets were separated according to the angle of squint, a constant rivalry between normal and anomalous correspondence impeded the performance of the test. Stereoscopic targets superimposed on the screen were seen singly; fusional movements occurred when targets were converged up to 10 arc degrees or diverged up to 5 and 6 arc degrees, but, again, there was no stereopsis; there was an alternate suppression of the disparate elements.

IV. PRINCIPLES OF TREATMENT OF ANOMALOUS CORRESPONDENCE

The anomalous sensorial retinal relationship is a condition produced by the simultaneous stimulation of the two retinas when the eyes have an abnormal relative position. On the basis of this definition, one can logically divide the methods which might be expected to restore the normal retinal relationship into four groups: (1) methods excluding one eye from the act of vision (occlusion); (2) methods restoring the normal relative position of the eyes (operations); (3) methods pro-

ducing bifoveal stimulation by optical means (prisms); (4) methods employing the simultaneous stimulation of selected retinal areas (orthoptic exercises).

1. METHODS EXCLUDING ONE EYE FROM THE ACT OF VISION (OCCLUSION)

If one eye is permanently excluded from the act of vision by occlusion for a prolonged period, there is no binocular stimulation, and one of the main factors maintaining anomalous correspondence is avoided. I have not made a systematic study of this subject, and my experience is restricted. I am, therefore, unable to state with certainty whether or not occlusion is of definite help in breaking down the anomalous correspondence. However, I do not question that it is frequently a valuable therapeutic adjunct. I have seen a number of cases in which occlusion of the leading eye, instituted for the purpose of improving the vision of the deviated eye, has led in a relatively short time to a notable improvement in the condition of the sensorial retinal relationship. Similar observations were made by Hoorens.[45] Chavasse[46] claimed that this method may be expected to accomplish more than any method of intermittent stimulation, and Pugh[47] stated the belief that preoperative and postoperative occlusion were absolutely essential in the treatment of anomalous correspondence.

As an illustration, I am reporting a case which clearly demonstrates the beneficial influence of occlusion.

CASE 23.—E. L. T., a white girl 8 years of age, came from a highly hyperopic family on the maternal side. It was noticed that her right eye turned in when she was 2 years of age; she had worn glasses since the age of 4 years.

Refraction and Visual Acuity.—Right eye: $+6.00$ D. sph. $\bigcirc +1.75$ D. cyl., axis $90 = 20/100$; left eye: $+5.50$ D. sph. $\bigcirc +1.00$ D. cyl., axis $90 = 20/20$.

Retinal Correspondence.—The cover test revealed 12 arc degrees of convergent strabismus of the right eye. In the double image test, the double images coincided and followed prism displacement in all directions. In the after-image test, the positive and negative after-images were seen thus, indicating anomalous correspondence adapted to the angle of squint. R —— —— L

After she had worn an occluder on the left eye for one month, the visual acuity of the right eye improved to $20/70 - 2$; there was no change in the angle of squint or in the localization of the after-images. In the double image test there was now an uncrossed diplopia of 4 arc degrees with either eye fixating. After two more months of wearing the occluder, vision in the right eye had improved to

45. Hoorens: Strabismes Concomitants, Bull. Soc. belge d'opht., 1939, no. 78, p. 10.

46. Chavasse, F. B.: Tests for Secondary Correspondence in Squint, Tr. Ophth. Soc. U. Kingdom **55**:482, 1935.

47. Pugh, M. A.: Squint Training, London, Oxford University Press, 1936.

20/50; the angle of squint still showed 12 arc degrees of convergence; in the double image test there was an uncrossed diplopia of 4 arc degrees, but the after-image test now showed normal localization of the after-images. Occlusion was continued again for two months; after that vision in the right eye had improved to 20/40; in the cover test the localization of both the double images and the after-images was normal. The patient was instructed to leave the occluder off and to return in two months, but she did not return for one year and nine months. When she was seen again, vision in the right eye had regressed to 20/200; the angle of squint was 6 arc degrees of convergent strabismus in the right eye. In the double image test, with the right eye fixating there was 6 arc degrees of uncrossed diplopia; with the left eye fixating there was no horizontal displacement. In the after-image test the positive and negative after-images were localized as shown in the diagram. R | —— —— L |

She wore again an occluder over the left eye, and after three months she had a corrected vision of 20/50 — 2 in the right eye; the localization of both the after-images and the double images was normal. With continued occlusion for five months longer vision in the right eye improved to 20/30 + 2; the retinal correspondence remained normal.

I believe this case to be of particular interest to the theory of anomalous correspondence. It demonstrates that anomalous correspondence can in suitable cases be broken down by occlusion, as proved in this case by the experiment which the patient unwittingly performed by leaving the occluder off for nearly two years and permitting a relapse into anomalous correspondence. But the case also demonstrates how accurately some highly adaptable persons adjust their sensorial retinal relationship to the existing neuromuscular conditions. When the patient was first seen, she had an angle of squint of 12 arc degrees; later the angle of squint was 6 arc degrees; in both instances she was sensorially fully adapted to the angle of squint. After she had left the occluder off, the only suggestion of the period of reawakened normal correspondence, produced by occlusion, with the normal localization of the double images when the patient fixated with the usually deviated eye.

Not all patients are as adaptable as the one in the case just discussed. It is not surprising, therefore, that I have seen a large number of patients in whom occlusion of the better eye, carried out for months, had no influence whatever on the sensorial retinal relationship. Travers [34] had a similar experience in 5 cases, in which alternating occlusion of one eye over an average period of four and a half months was completely ineffective. One is forced to conclude that the same factors which modify the establishment of anomalous correspondence and influence its spontaneous postoperative development in the individual case are also active when occlusion is carried out.

In evaluating monocular occlusion as a therapeutic means for the correction of anomalous correspondence, one must keep in mind that

it is a negative rather than a positive procedure. Simultaneous binocular stimulation is prevented, but nothing is done to further actively the reestablishment of the normal sensorial relationships. This is attempted by the methods which are now to be discussed.

2. METHODS RESTORING THE NORMAL POSITION OF THE EYES (OPERATIONS)

If the biretinal stimulation is to restore the normal sensorial relationship between the two eyes, then the stimulus must fall on such areas in the two retinas that the awakening of normal correspondence is made possible. In other words, the position of the eyes must be such that an object point fixated with one eye is also imaged on the fovea of the other eye. In most instances this can be achieved only by operation.

Travers,[34] as well as other authors, have stated the opinion that operation is the most effective method so far devised for dealing with anomalous correspondence. Indeed, there is no doubt that development in the direction of normal correspondence frequently takes place after surgical intervention. The ideal goal—a stable normal retinal relationship evident in all tests—is, however, only rarely achieved.

What is the reason for this? Strabismus is a deep-seated disturbance of the neuromuscular apparatus of the eyes. Operations on the ocular muscles can affect directly only the mechanical conditions. These operations are crude procedures when compared with the fineness of the neuromuscular mechanism which comes into play in binocular fixation. An absolute parallelism of the visual lines for distance is hardly ever achieved by operation and is often not desired. Since normal fusional amplitudes are almost always absent in patients with strabismus, such persons are unable to correct the small deviations of the visual lines which remain after successful operation. Consequently, the condition for regaining normal correspondence, the simultaneous stimulation of the two foveas by the fixation point, is lacking.

Another factor which frequently works against the spontaneous reestablishment of normal correspondence is the age at which operation is performed. As far as the cosmetic result is concerned, there is no upper age limit for the operation; but there is no doubt that the prospect for a satisfactory functional result decreases rapidly with the age of the patient. A patient who is operated on in his teens is much less likely to regain spontaneously normal correspondence and binocular vision than one who is operated on at the preschool or the grammar school age. This has been emphasized by many writers, and with regard to retinal correspondence, particularly by Montalvan.[48] Travers [34] published con-

48. Montalvan, P.: El tratamiento ortóptico del estrabismo concomitante, Rev. cubana de oto-neuro-oftal. **6**:97, 1937.

vincing figures on this subject, and he also showed that not only the age of the patient at the onset of the strabismus but also the "percentage of life" during which the patient squinted has to be considered in this respect.

Yet one still hears and reads frequently that one should not operate for strabismus before the patient is 12 or 14 years of age. This is erroneous. Every child with strabismus who comes to a physician's attention should have his eyes straightened before entering school or shortly thereafter. There are many reasons for advocating such a policy; the better prospect for a good functional result is one of the more important ones. The danger of a postoperative divergence can be avoided by proper choice and proper performance of operation and should not be a deterrent to early surgical intervention.

3. METHODS PRODUCING BIFOVEAL STIMULATION (PRISMS)

In order to produce the image of the fixation point simultaneously on the two foveas of a squinting patient by nonsurgical means, prisms may be employed. The use of prisms in the treatment of strabismus has been strongly advocated by some authors, particularly Sattler,[49] who has seen good results from prisms as strong as 22△. Other authors have found them useful. Travers[34] applied them with special regard to overcoming anomalous correspondence but found the results in his 4 cases most discouraging. The prisms were heavy, unsightly and expensive; the children did not like them, and the parents were resentful. In 1 case Travers noted an increase in the angle of squint after the prisms were worn.

Travers' material is too small to justify one in drawing final conclusions from it. Prisms can be used, of course, only when the angle of squint is relatively small, but there is no objection to their use on theoretic grounds. If the patient is at all capable of regaining normal correspondence, the correct position of the images on the retina will undoubtedly be helpful. It must be admitted, however, that prisms *in praxi* are not always beneficial, and that they can even be detrimental. In a number of instances I have seen an occurrence similar to that described by Travers, in which the angle of squint increased as a result of the wearing of prisms. The amount of increase usually corresponded to the amount of prism power prescribed. Since the prisms were given only in cases in which the angle of squint was small (5 to 6 arc degrees) and corresponded to it in strength, this usually meant that the angle of squint had doubled as a result of the wearing of prisms.

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49. Sattler, C. H.: Erfahrungen über die Beseitigung der Amblyopie und die Wiederherstellung des binokularen Sehakts bei Schielenden, Ztschr. f. Augenh. **63**:19, 1927.

This interesting observation may be explained as follows: Patients with strabismus try to avoid simultaneous macular perception. If they are operated on with success, the mechanical conditions are altered in such a way that the faulty innervational factors which remain operative, at least for some time, are unable to produce a deviation. The patient successfully operated on will either yield and return at least partially to sensorial normalcy or will acquire sensorial anomalies adapted to the new motor conditions. If the bifoveal stimulation is achieved by the use of prisms instead of by operation, the faulty innervational factors will continue to operate on the faulty mechanical conditions present in every case of strabismus. As a result, the situation will be aggravated. In order to avoid bifoveal stimulation, the eyes turn until the same distribution of the retinal stimuli is reached which existed prior to the use of prisms. Consequently, the patient now has the same angle of squint with the prisms which he had before wearing them.

Such experiences should not discourage the use of prisms. They are valuable, particularly for the correction of vertical deviations. But it would be wrong to rely solely on prisms for the therapy of anomalous retinal correspondence. More active methods must be sought to encourage the establishment of normal correspondence.

4. METHODS EMPLOYING THE SIMULTANEOUS STIMULATION OF SELECTED RETINAL AREAS (ORTHOPTIC EXERCISES)

When the image of the fixation point is moved over the retina of the deviated eye, an anomalous localization of the double image may suddenly be replaced by normal localization. Bielschowsky [31a] observed this in examining squinting patients with rotary prisms. When testing patients with the movable projection instrument,[15] I have seen it happen time and again that normal correspondence would suddenly appear when a small light spot was moved to and fro on the screen in such a way that it was imaged on the region of the macula of the deviated eye.

The instability of the anomalous retinal correspondence and the fact that normal correspondence may be elicited by moving the image of an object over the macular area of the deviated eye are made use of in orthoptic training. It is known as "retinal massage."

According to Linksz,[50] the value of this treatment lies in the reconditioning of attention. As soon as the patient is able to catch two patterns in one act of attention, which is best achieved by flashing lights or by motion, they will appear in one and the same direction. This is undoubtedly an interesting explanation; the importance of attention in all functions of vision is paramount (Hering). It must not be overlooked, however, that for attention to be effective there must be a physiologic basis—in this instance the presence of common visual directions.

50. Linksz, A.: Objectives of Orthoptic Examination and Treatment, Am. J. Ophth. **26**:552, 1943.

Since I am dealing here only with the principles of treatment of anomalous correspondence, I shall not go into a discussion of the details of the orthoptic technic. But it must be pointed out that opinions about its value vary from complete denial to enthusiastic affirmation. Chavasse [51] emphatically denied the possibility that a cure of anomalous correspondence could be achieved by means of orthoptic exercises, and Fowler [52] found that orthoptic training was of no value either preoperatively or postoperatively in cases of abnormal retinal correspondence. On the other hand, one hears statements from some orthoptists that they effect a cure in virtually every case of anomalous correspondence. The truth, no doubt, lies between the two. It surely depends largely on the skill of the orthoptist what result will be achieved, but the over-all handling of the cases is just as important.

To awaken the normal sensorial relationship once, twice, or even three times a week for the short period during which the treatments

TABLE 1.—*Influence of Orthoptic Treatment in Anomalous Correspondence in Operative Cases*
(After Berens, Elliot and Sobacke [55])

		Before Operation		After Operation	
Orthoptic Treatment	Retinal Correspondence	Number of Cases	Percentage	Number of Cases	Percentage
None	Normal	61	42	64	45
	Anomalous	83	58	80	55
Postoperative only	Normal	83	36	65	79
	Anomalous	30	53	18	21
Before and after operation	Normal	73	75	80	82
	Anomalous	25	25	17	18

are given, and to allow the patient to relapse into his faulty visual habits the rest of the time, will certainly not produce a cure of anomalous correspondence.[53] Provision must be made to prevent the patient permanently from the wrong use of his eyes.

The best method to achieve this is the operative correction of the angle of squint. All authors who agree that orthoptic training is beneficial in the therapy of anomalous correspondence are also agreed that it should be given in conjunction with operative procedure.[54]

51. Chavasse (footnotes 27 and 46).

52. Fowler, M. J.: Value of Orthoptic Fusion Training Exercises in Strabismus and Related Conditions, Arch. Ophth. **28**:507 (Sept.) 1942.

53. A word of warning must be inserted against the indiscriminate use of home exercises with stereoscopes. I have seen a number of patients in whom anomalous visual habits had become thoroughly established owing to the uncontrolled use of a stereoscope.

54. T. Keith Lyle (Lyle, T. K., and others: Orthoptic Training, Tr. Ophth. Soc. U. Kingdom **59**:491, 1939) expressed the belief that "the persistence of

(Footnote continued on next page)

In this connection, the figures published by Berens, Elliot and Sobacke [55] are of particular interest. These authors followed a large number of cases and found that operation alone hardly influences the condition of the sensorial retinal relationship. A return to normal retinal correspondence is found in a substantial number of patients if the operations are combined with orthoptic procedures. The figures given by these authors are reproduced in table 1.

In concluding this survey of the principles of treatment of anomalous correspondence, it can be stated that there is no one certain panacea for all cases. In fact, the treatment of this condition is one of the most difficult problems in ophthalmology. Even the most skilful application of all means at one's disposal leads to a permanent cure in only a relatively small number of cases. Again, all the factors which lead to the establishment of anomalous correspondence—the age of the patient, the individual adaptability and the completeness with which the normal correspondence is repressed—play a decisive role in the success of the treatment.

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abnormal correspondence in spite of diligent orthoptic treatment over a period of two to three months indicates the necessity for operation in the hope that the retinal correspondence which occurs in some 40% of the cases may become normal."

55. Berens, C.; Elliot, A. J., and Sobacke, L.: Orthoptic Training and the Surgical Correction of Strabismus: A Comparative Study of Binocular Vision in 324 Surgical Cases With and Without Orthoptic Training, Am. J. Ophth. **24**:1418, 1941.

(To Be Concluded)

News and Notes

EDITED BY DR. W. L. BENEDICT

UNIVERSITY NEWS

The University of Michigan Department of Postgraduate Medicine, Department of Ophthalmology.—The twenty-first annual intensive postgraduate course in otolaryngology and ophthalmology will be given from April 24 to April 30, at the University of Michigan Medical School, Ann Arbor, Mich., by the resident staff and the following guest lecturers: Dr. Albert D. Ruedemann, Cleveland; Dr. Dohrmann K. Pischel, San Francisco; Dr. Edmund B. Spaeth, Philadelphia; Dr. Jack S. Guyton, Baltimore; Dr. Elmer L. Whitney, Detroit, and Dr. Willis S. Knighton, New York.

Applications or inquiries should be sent to the Department of Postgraduate Medicine, University Hospital, Room 2040, Ann Arbor, Mich. Owing to the difficulty of obtaining accommodations, it is wise to write at once for reservations to the Michigan Union, University of Michigan, Ann Arbor, or the Women's League, University of Michigan, Ann Arbor.

GENERAL NEWS

Optical Aids for Subnormal Vision.—The Committee on Sensory Devices of the National Research Council has available a limited number of reprints of a condensation of the "Report on a Survey of Optical Aids for Subnormal Vision," by V. S. Ellerbrock, recently published in the *Journal of the Optical Society of America*. There are also available a limited number of copies of the original, unabridged, report. This report, which was prepared to guide the committee in formulating a program of research, deals with the theory and practical aspects of telescopic spectacles, loupes, reading glass magnifiers and projection systems, as well as with recommendations for possible improvements in these devices. Copies of either of these reports will be mailed to professionally interested persons, on request to the Dartmouth Eye Institute, 4 Webster Avenue, Hanover, N. H.

Oregon Academy of Ophthalmology and Otolaryngology.—The eighth annual spring postgraduate course in ophthalmology and otolaryngology will be held in Portland, Ore., April 7 to 12, 1947. The Oregon Academy of Ophthalmology and Otolaryngology and the University of Oregon Medical School have arranged a program, and Dr. John Dunnington, professor of ophthalmology at Columbia University College of Physicians and Surgeons, New York, and Dr. George Shambaugh, professor of otolaryngology at Northwestern University Medical School, Chicago, will be the speakers. There will be lectures, clinical demonstrations and ward rounds. Preliminary programs will be available about March 1. Additional information may be procured from Dr. Harold M. U'Ren, secretary, 1735 North Wheeler Avenue, Portland 12, Ore.

American Orthoptic Council.—The next examination for technicians by the American Orthoptic Council will be held in September and October 1947. The written examinations will be held at various cities in the country on Friday, Sept. 12, 1947. Only candidates passing the written examinations will be permitted to take the oral and practical tests, to be given in Chicago, Saturday, Oct. 11, 1947.

Applications on the official form must be received before July 1, 1947.

Communications may be addressed to the American Orthoptic Council, 23 East Seventy-Ninth Street, New York 21.

Annual de Schweinitz Lecture.—The 1947 de Schweinitz Lecture will be given on Thursday, Nov. 20, 1947, in Philadelphia, by Dr. Bernard Samuels of New York, whose subject will be "Necrosis of Intraocular Tissues."

SOCIETY NEWS

Election of Officers, American Academy of Ophthalmology and Otolaryngology.—At the meeting of the American Academy of Ophthalmology and Otolaryngology in October 1946 the following officers were elected: president, Dr. Alan C. Woods, Baltimore; president elect, Dr. C. H. McCaskey, Indianapolis; executive secretary-treasurer, Dr. W. L. Benedict, Rochester, Minn.; secretary for otolaryngology, Dr. O. E. Van Alyea, Chicago; secretary for ophthalmology, Dr. Algernon B. Reese, New York; secretary for instruction in otolaryngology, Dr. Dean M. Lierle, Iowa City; secretary for instruction in ophthalmology, Dr. A. D. Ruedemann, Cleveland; secretary for home study courses, Dr. Lawrence R. Boies, Minneapolis; secretary for public relations, Dr. Erling W. Hansen, Minneapolis. Councillors elected were: Dr. C. H. McCaskey, Indianapolis; Dr. James M. Robb, Detroit; Dr. C. D. Blassingame, Memphis, Tenn., and Dr. W. Ivan Lillie, Philadelphia.

Asociación para Evitar la Ceguera en México.—The Society for the Prevention of Blindness in Mexico will hold a third scientific week from Aug. 11 to Aug. 16, 1947, in México, D.F. Papers are invited and should be in the hands of the Asociación para Evitar la Ceguera en México, Gómez Farias 19, México, D.F., not later than July 10, 1947.

Correspondence

TEACHING OF BASIC SCIENCES IN OPHTHALMOLOGY

To the Editor.—I have read with great interest the proof of Dr. Cogan's article on "Aims and Aids in the Teaching of Basic Sciences in Ophthalmology."

Dr. Cogan's insistence that "emphasis should be put on the teachers and the course organized around them" is admirable. His outline of the material to be covered in the basic sciences cannot but be helpful to any administrator organizing such courses, and little exception can be taken to the fundamental value of the program he has outlined. It is immediately obvious, however, that, bearing in mind the qualifications of instructors and the subject matter to be covered, such courses in basic sciences can be given only in medical centers where ophthalmology is a major department and the necessary teaching personnel is available. Even in such centers the content of these courses will almost undoubtedly vary according to the individual interests, talents and opinions of the teaching staff. This is well illustrated by the material suggested by Dr. Cogan for the course in physiology—subjects in which Dr. Cogan himself is preeminently interested and in which his own investigations have been most noteworthy.

Granted that the content of the courses given in various ophthalmologic research centers will vary considerably according to the qualifications and interests of the different faculties, there are still several questions to be considered. First, what is the value of such instruction to future interns in the average isolated ophthalmic hospitals? Second, can all the men who take these courses with the idea of becoming ophthalmologists ultimately be placed in proper internships in ophthalmology? Third, in the larger ophthalmologic centers, should this instruction be given preliminary to the internship, or should it be given as an integral part of the first year's training?

In answer to the first of these questions, unhesitatingly I should answer that such preliminary training would be of value to the future interns in the isolated ophthalmic hospitals and in the end would raise the standards of ophthalmology practiced in such hospitals. In many instances, such a course in the basic sciences would be the one opportunity of such interns to obtain insight into basic scientific ophthalmology. Even though the prospective ophthalmologist may be better grounded in the basic sciences than his future preceptors, and so be liable to a rude awakening when he begins his actual clinical training, nevertheless, the general level of ophthalmologic practice will be considerably raised by this program.

Concerning the second point, however, one cannot but harbor grave doubts. If entrance to these courses in the basic sciences is limited to men with the proper scientific background and to men who have already obtained internships in ophthalmology, full approval of the program is instantaneous. However, at the present time every ophthalmologic

institution is deluged with applications from would-be ophthalmologists. The reasons for this are obvious. First, in addition to the normal number of recent graduates who wish to become ophthalmologists and heretofore have comfortably filled the existing internships, there are a number of men who under normal conditions would have specialized in ophthalmology several years ago but have been delayed in starting their training by their military service. Second, there are a great number of poorly trained and educated men who have completed their military service, are dissatisfied with their former medical practice and now take the opportunity offered by the G. I. Bill of Rights to enter a speciality which they correctly believe to be lucrative and erroneously believe to be easy. The great majority of the latter group are poor material and even under normal conditions would have great difficulty in obtaining hospital appointments. Under present conditions their chances of so doing are minimal. It is unfortunate, but true, that as a rule the applications of the latter group wind up with the statement that they have been accepted for such and such a course in the basic sciences and will be available for appointment on a certain date. I have grave doubts whether any appreciable number of this group will ever succeed in obtaining the later necessary clinical training. When one considers the limited number of ophthalmologic internships available and the present overwhelming number of applicants, it would appear that many of the graduates of these courses are doomed to disappointment in their desire to become properly qualified ophthalmologists. Therefore, while I am in full approval of Dr. Cogan's proposition that men later entering isolated ophthalmic hospitals should have this course in the basic sciences as a preliminary, I feel strongly that admittance to such basic courses should be limited to men who have either obtained their ophthalmologic internships or who have fair prospects of ultimately being properly placed.

On the last question I have raised, namely, the wisdom of giving these courses as a preliminary to internship in the larger ophthalmologic research and teaching centers, I am in complete disagreement with Dr. Cogan's opinion that the courses should be taken by a student just prior to his residency in ophthalmology if possible, but in any case not during his residency. To my mind, the future ophthalmologist is vastly better able to appreciate the content of the basic science training if he is surrounded at the same time with evidences of its clinical application and if he realizes the necessity of a proper scientific foundation for his clinical work. For example, a student of ophthalmic pathology is more able to appreciate the significance of histologic changes when he has some inkling of the varying clinical course of the disease he is studying. Further, a student receives a stimulus from serving under an instructor in the wards of a hospital and then following the same man to his laboratory for basic training in the applied sciences. To see the knowledge he gains in his basic courses—physiology, bacteriology, chemistry, anomalies of ocular movements and stereopsis, anatomy and other sciences—directly applied to the actual care of the patient is to my mind much better training than straight didactic or laboratory instruction, divorced from clinical work.

In the larger ophthalmologic institutions such combined basic scientific and clinical instruction can be readily arranged. The internship

runs throug.i an entire year, and practically all men continue for an additional year or longer. I believe the wiser plan for the training of ophthalmologists is to spread the basic work in anatomy, pathology, physiology, chemistry, physiologic optics, muscular anomalies, etc., throughout the first year of training and to continue into the second year more advanced work in pathology, bacteriology and other subjects which may be of especial interest to the individual student, thus allowing the young ophthalmologist an opportunity, within certain definite limits, to develop along his own natural inclinations.

ALAN C. WOODS, M.D., Baltimore.

Johns Hopkins Hospital.

Having been interested in ophthalmologic education and the training of ophthalmologists for twenty-two years, it is my hope that the article by Dr. Cogan will act as a stimulus to better teaching. While I am in general agreement with the ideas expressed in this paper, I believe that a few points will bear discussion.

It is well known that many clinicians have an inadequate knowledge of the basic sciences as applied to ophthalmology, having obtained their training by preceptorships or in an institution where only clinical practice is taught. Any courses in the basic sciences added to such teaching are of inestimable value.

For many years studies in the basic sciences have been an important part of the four year period of training in ophthalmology at the State University of Iowa College of Medicine. It has been felt that one not grounded in such subjects cannot be a good clinician. In addition, the residents have been encouraged to enhance their knowledge of internal medicine, neurology and certain phases of pediatrics.

I am in agreement with Dr. Cogan in his belief that the teachers "either make or break the course." Most assuredly, the instructors should be clinicians, since only they can emphasize important medical and surgical points.

I cannot agree in the belief that the basic sciences should be studied necessarily prior to the residency in ophthalmology, and in no case during the period of residency. From long experience, it is felt that the preferable method is to train interns in the basic sciences and in clinical ophthalmology concurrently, preferably during the first two years of residency. Taught in this manner, the student is more stimulated to study, and by daily application, for example, of embryology, anatomy, bacteriology and pathology to clinical practice he is made to realize the importance of a thorough knowledge of the basic sciences. As a consequence, an inclination to study some of the "dry" subjects is created. It is the experience of my colleagues and myself that there is much more interest in the basic sciences when they are applied daily to clinical problems. For example, in the course in bacteriology, the student spends six months in the study of external diseases and bacteriology, during which time he makes smears, cultures and other laboratory tests on each patient seen in the clinic. Thus, the clinical and laboratory findings are correlated, and the entire picture is fixed in mind. Likewise, in the training in pathology a patient with malignant melanoma, for example, is examined in the clinic, and after removal of the eye gross and microscopic studies are made.

As to the amount of training in the basic sciences, it seems that twelve weeks is not sufficient; six months would be preferable.

However, let there be training in the basic sciences, whether it is during, before or after the residency. More interest and willingness to sacrifice on the part of those who teach will result in a better profession.

C. S. O'BRIEN, M.D., Iowa City.

I heartily approve of the basic course described by Dr. Cogan. It is difficult to see how any one could disapprove of it, since "the proof of the pudding is in the eating" and the course has already been given so as to satisfy its students and teachers. Facts which Dr. Cogan did not mention, but which I understand to be true, are that the course has been limited to thirty members, that many more applications have been received than could be accepted and that the course has been financed by tuition fees. For several reasons, the course should be of benefit to ophthalmologists and to ophthalmology. It will attract desirable men and exclude or discourage those obviously unsuited to become ophthalmologists. It will stimulate qualified men to undertake ophthalmologic research, and it will produce a reserve of future teachers. It will induce ophthalmologists who have taken it to read the literature in their field and will enable them to do so with pleasure and profit.

It is probable that at the outset the teachers will learn more from the course than will the students and that later the teachers will lose their enthusiasm. By the time they do so, however, new teachers may be available from the ranks of their former students.

In conclusion, I cannot refrain from noting that a paper which I wrote twenty-eight years ago (Suggestions Regarding the Teaching of Ophthalmology, ARCH. OPHTH. **49:** 1 [Jan.] 1940), and which I read before the New York Academy of Medicine, Section of Ophthalmology, is just beginning to bear fruit.

F. H. VERHOEFF, M.D., Boston.

395 Commonwealth Avenue.

I have read with interest the article by Dr. David G. Cogan entitled, "Aims and Aids in the Teaching of Basic Sciences in Ophthalmology." There is no question in my mind but that a study course in the basic sciences as applied to the eye will become a regular part of every ophthalmologic residency in the country. The experience gained in organizing the course at Columbia University and in participating in the course at Harvard and in the two courses sponsored by the Ophthalmological Study Council has given me a number of impressions which I should like to discuss in connection with Dr. Cogan's paper.

I agree with Dr. Cogan that only the exceptional person acquires adequate training in the basic sciences as applied to ophthalmology without an organized course. Without such a course the average resident enters ophthalmology with only a superficial knowledge of the applications of the basic sciences to the eye.

As Dr. Cogan says, the success of the course depends in large measure on the faculty, and it is in connection with the faculty that most of the difficulties have arisen. In the course at Columbia it was originally planned that the basic science departments themselves should

furnish the principal instructors, these to be supplemented by instructors from the department of ophthalmology itself who had had special training in the basic sciences but who were primarily clinical ophthalmologists. It was soon found that unless the instructors from the basic science departments had developed special interests in the eye their management of the course proved generally unacceptable to the residents. These nonophthalmologic instructors tended to offer simply a review course in the basic sciences, without making any attempt to apply their knowledge to specific problems in ophthalmology. Generally speaking, it is not possible in any one school to assemble instructors who have special ophthalmologic interests in all the fields of the basic sciences. Some sort of compromise must therefore be made. Perhaps one method would be to stimulate interest in ophthalmic problems among the members of the basic science departments by offering adequate remuneration to the instructors for their time and effort. An alternative possibility would be to bring in instructors from other schools. Bringing in outside help has the advantage that superior instructors can be chosen who will be able to maintain the interest of the residents, but there is the great handicap that such instructors must in general rely wholly on didactic instruction, without the advantage of supplementary laboratory work. I agree thoroughly with Dr. Cogan that the basic course must have laboratory instruction in addition to the didactic work if it is to be truly successful.

There must be a happy balance between didactic instruction and laboratory instruction. A course heavily weighted on either side will be unsatisfactory. In this connection, it is of interest to refer to the two courses sponsored by the Ophthalmological Study Council, in which lack of adequate laboratory facilities was balanced in large part by the superiority of the teaching staff. This course, unlike the university-sponsored courses, had the benefit of outstanding instructors in each subject, imported from all parts of the country, whose enthusiasm and prestige were able to compensate in large part for the absence of laboratory facilities. It should be mentioned, however, that a certain amount of laboratory work was made available in the second of the Council's two courses. At the other extreme is the course too heavily weighted on the laboratory side, in which much valuable time is lost in conducting useless experiments and with which the students become exhausted and bored. Much greater skill is required on the part of the instructor in handling the laboratory demonstrations than in ordinary didactic instruction. It is often better to have the experiment performed by the instructor in front of the class than by the individual members of the class. Students in ophthalmology should not be returned to the freshman level of medical study.

The value of weekly examinations was well shown in the courses of the Ophthalmological Study Council. Knowledge that the examination was to be given on the material currently presented served as a healthy stimulant to the student, and returned papers with corrections served to point up deficiencies. The grades in these courses should be saved for presentation to the American Board of Ophthalmology, to be used as an aid in determining the fitness of applicants for examination.

I agree with Dr. Cogan that the proper time for the basic science course is just prior to the beginning of the residency. Experience at Columbia University showed that it was highly undesirable to have the course run simultaneously with the clinical work. Inevitably, calls from the wards and clinic obtained priority over calls from the course. This does not mean in any sense that training in the basic sciences should be discontinued during the residency. Ocular pathology, for example, is a subject which must have continuous application, as in weekly pathologic seminars, to enable the resident student to correlate his clinical and pathologic observations. Ophthalmic bacteriology is another subject which must have continuity and is best taught by requiring the resident to participate in a clinic for external diseases and to make his own cultures and microscopic slides.

Finally, every effort should be made in the university eye clinic to turn the interests of the younger men toward the basic sciences. In the past, pathology has received the greatest attention, but there is no reason that each university staff should not have an ophthalmologist qualified to teach and do experimental work in each of the basic sciences. There should be no hesitancy in calling on the basic science departments themselves for aid in the course, but I wish to stress again my belief that only exceptionally can the nonophthalmologic instructor in the basic sciences furnish the liaison between his science and ophthalmology that is absolutely essential.

PHILLIPS THYGESON, M.D., Los Altos, Calif.

P. O. Box 622.

I was very much interested in Dr. Cogan's article on the teaching of basic sciences in ophthalmology.

The outline is that of a truly basic course and is more comprehensive in the fundamentals than is usual in such courses. Any university that offers similar studies will be delighted with the outline presented. The division of hours is somewhat like that given at Washington University School of Medicine.

Of particular value is the apparent participation of the student in the laboratory work. Not only would twelve weeks of purely didactic teaching be unbearable, but the material would be poorly absorbed. It is only by delving into subjects with hands and eyes, as well as ears, that true understanding is gained and facts and theories are digested sufficiently for their retention.

My criticism of a purely basic course that does not include pathology and refraction is that it does not prepare a man adequately for the residencies that are now available in nonteaching institutions, since in most of these hospitals there is one to teach such subjects satisfactorily. The result is usually that the resident in ophthalmology learns his refraction by "hit or miss" methods, reading textbooks and occasionally picking up a few words of advice from a busy visiting staff ophthalmologist. He generally gets no instruction at all in pathology. Other subjects might be mentioned, such as muscle studies, orthoptics and practical perimetry, which need to be taught personally. It is agreed that these are not basic subjects, but they cannot be picked up and well understood without more definite instruction than a resident is likely to get in most hospitals.

For these reasons, it has seemed to me that the basic sciences in ophthalmology should be taught along with the clinical instruction. Therefore, at Washington University the so-called basic course, of eight months, has been a combination of basic and clinical training, approximately two hours a day being devoted to the basic work and six hours to clinical studies. This, to me, is the ideal arrangement, and I strongly favor it when possible.

The giving of a splendid basic course, such as Dr. Cogan has outlined, is indeed of great value, and the intelligent student will be able to build satisfactorily on it. But he will be indeed fortunate if he can later find a residency where he will receive systematic instruction in the clinical subjects.

LAWRENCE T. POST, M.D., St. Louis.

Washington University School of Medicine.

The aims of the basic science course in ophthalmology which Dr. Cogan has outlined are ideal. Any good student fortunate enough to take such a course given by Dr. Cogan and his associates should not only be thoroughly grounded in fundamental subjects but should also have acquired some knowledge of experimental methods. Association with such a group could not help but stimulate his curiosity, and it is more than likely that from it many top-ranking clinicians with an investigative turn of mind would eventually be produced. One cannot emphasize too strongly, however, as Dr. Cogan has only modestly hinted, that the success of such a course depends entirely on the personnel of the department giving it. There are not many institutions in this country in which a similar group of men form a staff capable of presenting such a course and having sufficient time to conduct it personally. To be realistic, there are probably not more than six residencies in this country in an institution where such a course could be given.

I made the statement that any good student accepted for this course would be fortunate. By the term "good student" I mean one who is suitable. It must be recognized that not all physicians who wish to become ophthalmologists have the same objectives, interests or capabilities. The course which Dr. Cogan has outlined is designed only for those students of superior mental caliber who have an interest in the academic aspects of ophthalmology, as well as its practice, and who hope eventually to become associated with a teaching institution where research is done. For any other type of student the laboratory work in physiology proposed in this paper would be ill suited.

Fifteen years ago I organized such a course for the students in the graduate school of ophthalmology at the University of Pennsylvania. It was limited to the physiology of the eye. My thought was to have the students repeat in the laboratory some of the sound experimental work in the older literature which had yielded proved ideas incorporated in present day thinking, so that the student could see for himself how present conceptions had been arrived at. Considerable time and thought were expended on setting up a series of experiments which could be performed by a small class without much previous experience in laboratory work. The results were disheartening. Out of a class of approximately 15 men, there were 2 or 3 who may have benefited. The others carried out the laboratory instructions fairly satisfactorily but showed little understanding of what the experiment was intended to prove and

no interest or initiative in carrying the reasoning of the experiment further. Most of these men were good students, but their chief interest was in practical ophthalmology. They had had no laboratory experience, and their powers of reasoning from experimental data had never been developed. The failure was not theirs, but mine, in that I had not selected the type of man from the class who would have benefited.

I am skeptical, therefore, whether the course as outlined by Dr. Cogan will have very widespread usefulness. To be successful, it must be limited to just the type of man who benefits from this kind of instruction.

In the residency in ophthalmology at the University of Pennsylvania Hospital, the basic sciences are taught in the Graduate School of Medicine during the first eight months of the residency. While the students do laboratory work in anatomy, embryology, histology, pathology and physiologic optics, no labratory periods are given in either physiology or chemistry. By the time the resident has been with us for two years, my colleagues and I have had an opportunity to determine whether or not he is the type to do experimental work. The men showing the mental qualifications and interest are then selected in the third year, when they carry on research with the various members of the staff and eventually are given problems of their own.

To summarize, I believe Dr. Cogan's course is ideal if given by a staff similar to his to students whose mental capacities and interests are suitable. It will not have widespread application, because there are not many institutions where a similar group of trained teachers are to be found who have the time to give twelve weeks to the presentation of such a course. Further, the number of men who will be found suitable for this type of teaching is small.

FRANCIS HEED ADLER, M.D., Philadelphia.

313 South Seventeenth Street.

Dr. David Cogan's discussion of the "Aims and Aids in the Teaching of Basic Sciences in Ophthalmology" offers much valuable help to those who are planning the organization of such courses. I agree with him that an increasing number of institutions will require such training as a prerequisite to clinical residency. Of those institutions which do not insist that such training be completed before the appointment to the residency is made, an increasing number will require some such instruction as part of the resident training program. At every stage in training and practice those who have had such a review demonstrate its advantages.

With Dr. Cogan's aims I am in entire agreement. Two of his conclusions (relating to the teaching staff and the period of the course) will probably be challenged, but the difficulties which my associates and I have encountered in conducting a review of the basic sciences at Columbia have led us to share his convictions.

The Faculty.—It is evident that facilities for teaching a comprehensive review course in the basic sciences are at present to be found only in the large teaching centers. Since the other medical specialties are also interested in promoting training in the basic sciences for future residents in their specialties, several medical schools have organized

basic science faculties, usually operating under the dean or the associate dean in charge of graduate instruction. There is such a basic science faculty at Columbia University, and it was our hope to use this faculty, in common with the other specialties, for instruction in the basic sciences in ophthalmology. This hope has not been fulfilled. Members of the basic science faculty who were not ophthalmologists or who had not acquired special interests in this field did not seem to realize the problems associated with ophthalmology or to fulfil the highly specialized needs of the course. There was too much extraneous material unrelated to ophthalmology, and too often the teaching was simply of first or second year medical school caliber.

Another plan proposed the utilization of three or four full-time members of the ophthalmologic faculty to do all the teaching. In periods between basic science courses these faculty members would devote full time to laboratory direction or studies. This plan has serious disadvantages. It is difficult to find an adequate teaching staff with the deep interest in and enthusiasm for all the subjects to be covered. The teaching tends to become too didactic and academic.

In our experience, the use of members of the clinical attending staff who are actively practicing ophthalmology, supplemented by the assistance of the full-time nonclinical staff, has proved most satisfactory. It distributes the teaching over a large number of men and assigns to each the subjects in which he has special training and interest. At the end of each course reports received from faculty members on the caliber and performance of the students are evaluated, together with similar reports from students on the instructors and material, with a view toward modifying the content or arrangement of the subsequent course.

The Time.—I agree with Dr. Cogan that the course should be taken just prior to, but not during, the residency. If properly organized and conducted, the review course in the basic sciences is a full-time occupation for several months, and it is my feeling that it should not be undertaken when other demands on time and attention are likely to cause conflicts. By other demands I mean, for example, calls to the ward to take histories or make physical examinations, to perform laboratory tests or to act as assistant. The student should have maximum freedom from responsibility and maximum opportunity for diligent application. The pursuit and application of his basic science studies can and should be carried on into his period of residency, and many of the short items in the curriculum can well be placed in both the basic science and the resident training schedule.

Dr. Cogan's outline of the content of the Harvard course is practical and well balanced. At Columbia we assign a higher percentage of time to bacteriology and virus studies, a lower percentage to neurology and neurophysiology and a considerably higher percentage to miscellaneous studies (such as biostatistics, diagnostic tests, ophthalmologic histories and examinations and evaluation of clinical and scientific problems). Within moderate limits, the time assigned to each subject will vary with the facilities—faculty, clinic and laboratory—for teaching it. My feeling at present is that a good comprehensive review in the basic sciences can be given in a full-time four months' course,

of approximately eight hundred hours, about four hundred of which are given to lectures and laboratory work.

There is a wide divergence of opinion between those who take the "let them dig it out for themselves" attitude and those who believe that every conference hour should be carefully prepared for, summarized and evaluated. While one is not dealing with preparatory school students or medical undergraduates, I firmly believe that the amount of material to be covered in four months requires careful faculty preparation and considerable discussion. The faculty member is in a much better position to evaluate the present status of knowledge than is the student, particularly with reference to sources of material. At Columbia we allot about one-half the time (four hundred hours) to study periods, not counting evenings, and divide the other four hundred hours between laboratory work, with demonstrations, and lectures, conferences, discussions, quizzes and seminars. Didactic work may be supplemented with examinations, quizzes or, preferably, seminars, in which students prepare, discuss and defend theses. Six review periods are conducted by an administrative officer (we use the director of research), who can direct or encourage individual investigations into fields for which the student has special talent or training.

The preparation of laboratory outlines, including notes, notebooks, photographs, bibliographies and reprints in each subject, has proved of great help in systematizing the material covered. So many laboratory data (chemical formulas, preparation of stains, details of technic, optical equations and formulas and tabular data) are so easily twice learned and thrice forgotten that this material should be stored in a place where it is immediately available when needed. In this way, the student's mind and attention can be freed for more important aims: the development of a breadth of view, clear thinking and careful observation, with critical analysis or evaluation of what he sees, reads and hears.

LeGrand H. Hardy, M.D., New York.

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Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Congenital Anomalies

PERSISTENCE AND HYPERPLASIA OF THE PRIMARY VITREOUS. A. B. REESE and F. PAYNE, Am. J. Ophth. **29:** 1 (Jan.) 1946.

Reese and Payne attribute the increased frequency of retrolental fibroplasia to a lower mortality of premature babies. They describe four clinical types of this condition, and report 50 cases. They discuss these from the standpoint of diagnosis; the embryologic, pathologic and etiologic aspects, and treatment.

W. S. REESE.

CONGENITAL ANOMALIES FOLLOWING MATERNAL RUBELLA IN EARLY WEEKS OF PREGNANCY, WITH SPECIAL EMPHASIS ON CONGENITAL CATARACT. C. H. ALBAUGH, J. A. M. A. **129:** 719 (Nov. 10) 1945.

Albaugh reviews the literature and reports 9 cases of congenital abnormalities in the infant following an exanthem in the mother in the early weeks of pregnancy. The following summary is supplied: Available data suggest that 100 per cent of the mothers who contract rubella in the first two months, and approximately 50 per cent of those who contract it during the third month of pregnancy, will give birth to infants with congenital anomalies.

The commonest lesions in the infants are cataract, cardiac septal defects and patent ductus arteriosus, deaf-mutism and microcephaly.

Nearly all the infants are poorly developed and are feeding problems.

W. ZENTMAYER.

General

MOSCOW EYE HOSPITAL. A. USPENSKY, Brit. J. Ophth. **30:** 372 (June) 1946.

Uspensky gives a brief description of the Moscow Eye Hospital, one of the oldest ophthalmologic institutions in the country. It was founded one hundred and twenty years ago. The outpatient department is visited daily by 500 patients. The number of beds is 250. The hospital has adjunct clinics for thorough special examinations of the patients. It holds periodic and regular scientific conferences for exchanges of experience and maintains close contact with related institutions.

W. ZENTMAYER.

General Diseases

OXYCEPHALY ASSOCIATED WITH KLIPPEL-FEIL SYNDROME AND OTHER SKELETAL DEFECTS. A. L. PETER, Am. J. Ophth. **29:** 685 (June) 1946.

Peter reports 4 cases of mild oxycephaly in which skeletal defects were present. The chief complaint in all cases was inability to wear

the ordinary type of helmet. He presents these cases to show that this condition exists in mild form and shows few, if any, symptoms.

W. S. REESE.

OCULOGLANDULAR TULAREMIA. A. A. SINISCAL, Am. J. Ophth. **29:** 698 (June) 1946.

Siniscal reports 3 cases of proved oculoglandular tularemia, in all of which a domestic animal which had been previously ill was deemed the agent of transmission, although it was impossible to determine positively that the animal's illness had been tularemia.

W. S. REESE.

General Pathology

A CONTRIBUTION TO THE PATHOLOGY OF BOWMAN'S MEMBRANE. A. LOEWENSTEIN, Brit. J. Ophth. **30:** 317 (June) 1946.

Loewenstein studied the histologic changes in Bowman's membrane in a case of band-shaped corneal degeneration and in glaucomatous eyes, as well as the concretions in Bowman's membrane in a case of late changes following mustard gas (dichloroethyl sulfide) injury to the eye and in a case of hypertensive retinopathy. He concludes that precipitation of calcium phosphate in Bowman's membrane may be due to a slowing down of corneal metabolism. Carbon dioxide escapes; alkalosis sets in, and calcium phosphate is condensed in the tissue with the slowest metabolism, which is Bowman's membrane. The influence of light in this process of precipitation is likely. A calcified Bowman's membrane is an obstacle to the exchange of normal fluid from the epithelium to the anterior chamber. Its sequel is the establishment of an amorphous eosinophilic substance in front of Bowman's membrane, which was observed in a case of band-shaped corneal degeneration and in a case of late, progressive macular corneal opacities after mustard gas (dichloroethyl sulfide) poisoning. Increased intraocular pressure may be a further obstacle to the entrance of fluid into the inner eye. The frequency of hemispherical bodies in Bowman's membrane in cases of primary and secondary glaucoma may be due to the precipitation at this border zone. A case of arterial hypertension is described in which another form of purple-staining concretions was present in Bowman's membrane and in the superficial scleral layers. The precipitation may be a general metabolic deterioration of the ocular walls.

W. ZENTMAYER.

Injuries

AN ANALYSIS AND FOLLOW-UP OF 301 CASES OF BATTLE CASUALTY INJURY TO THE EYES. G. I. SCOTT and I. C. MICHAELSON, Brit. J. Ophth. **30:** 42 (Jan.) 1946.

Three hundred and one cases of battle injury to the eyes were analyzed and the men followed until they either were repatriated or had returned to duty.

Fifty-eight patients (19 per cent) had bilateral injury, 23 (76 per cent of the total number and 40 per cent of the men with bilateral injury) becoming certifiably blind.

In approximately 80 per cent of cases of injuries caused by grenades, land mines or booby traps the explosion occurred within 3 yards (2.7 meters). In approximately one third of cases of foreign bodies situated in the vitreous extraction was done with the electromagnet by the posterior route.

In 40 per cent of all cases of severe injury to the eye useful vision was retained, acuity being 6/12 or better in 20 per cent. In an additional 16 per cent, however, the defect was due to uncomplicated cataract, the eye being therefore potentially useful.

The final visual acuities in cases of perforation, contusion and concussion are compared, concussion being less destructive than contusion and perforation being considerably more serious than either in its effect on function.

A distinguishing feature is indicated between the clinical findings in cases of air-conducted and in cases of tissue-conducted concussion injuries to the globe. The pathogenesis of this distinction is suggested.

The principal causes of serious visual defect (6/60 or less) in cases of perforation, contusion and concussion are summarized. Infection appeared to be a negligible factor.

No case of sympathetic ophthalmia is recorded.

A follow-up study of 249 cases showed that over 60 per cent of the men returned to full duty.

W. ZENTMAYER.

AMNIOTIC MEMBRANE GRAFTS IN CAUSTIC BURNS OF THE EYE (BURNS OF THE SECOND DEGREE). A. SORSBY and H. M. SYMONS, Brit. J. Ophth. **30: 337** (June) 1946.

The authors feel that in the absence of control clinical or experimental evidence the results recorded here must be taken as an expression of clinical opinion, rather than proof. Most caustic burns are of the second degree. These burns show a localized and relatively superficial conjunctival lesion and a variable superficial corneal lesion. For these burns, which are both common and productive of much disability, grafting with amniotic membrane appears to offer a simple means of considerably reducing the normally protracted course of recovery and preventing both corneal and conjunctival complications. Thirty patients were treated with human amniotic membrane. Recovery was rapid, and there were few complications and sequelae. Grafting immediately or after one or two days is advocated for second degree burns of the eye.

W. ZENTMAYER.

Instruments

AN EXOPHTHALMOMETER FOR DIRECT MEASUREMENT. A. GORMAZ, Brit. J. Ophth. **30: 350** (June) 1946.

The instrument consists of a metal millimeter rule carrying one fixed and one movable vertical stem resting on the outer orbital canthi. A central movable vertical stem, calibrated in millimeters and terminating in a shallow cup, can be moved into position over the eye to give the measurement of the projection of the corneal apex beyond the level of a plane formed by the two orbital canthi. In no normal case has the summit of the cornea as determined by these readings been

less than 12 mm. above the fixed bony landmark of the outer orbital canthus. Generally the reading is 14 to 16 millimeters. The article is illustrated.

W. ZENTMAYER.

Lens

SIMULTANEOUS DETACHMENT OF THE CHOROID AND RETINA AFTER CATARACT OPERATION. H. ARRUGA, Barcelona, Spain, The Author, 1946.

1. The author corroborates the frequency with which the retinal detachment occurs at the same time as the choroidal one, as pointed out by Bonnet and Grand-Clément.

2. The posterior or lateral location of the retinal detachment is always next that of the choroid, a fact suggesting that the exudate, instead of occupying the subchoroidal space, is situated under the retina and raises it.

3. The retinal detachment disappears at the same time that the choroidal one does; therefore, the two have the same benign and transitory character.

4. The pathogenesis of the two kinds of detachment is probably the same, with the difference that the extravasated fluid collects in the subchoroidal space in the one and on the inner surface of the choroid in the other.

5. In 1 case in which a true detachment of the retina occurred, two and one-half months after the operation, the position of the tear was an indication of its lack of relation to the postoperative detachments of the choroid and retina.

HUMBERTO ESCAPINI.

CORNEAL SECTION AND SUTURES IN THE CATARACT OPERATION. H. ARRUGA, Barcelona, Spain, The Author, 1946.

The section in the limbus with conjunctival sutures heals quickly, but the union is not firmly closed against intraocular pressure and blepharospasm. The sutures are easily inserted and removed and if tied tightly fall out of themselves after six days. A stronger closing but a slower cicatrization of the wound is found when corneal or corneoscleral sutures are used. Very fine needles are necessary. The threads are sometimes difficult to extract. If the section is in the periphery and scleral, there is a tendency to hemorrhage from the vessels as they cross the anterior scleral region. When the incision is made in the limbus and the sutures include the cornea, sclera and a part of the conjunctiva, the union is solid, the healing is rapid and removal of the sutures is relatively easy.

ARNOLD KNAPP.

Methods of Examination

THE ULTRA-VIOLET OPHTHALMOSCOPE. J. DEMENT, Brit. J. Ophth. 30: 370 (June) 1946.

The instrument consists of a round mirror, either concave or plane. Mounted in the central perforation of the mirror is a small circular window of an ultraviolet opaque medium, such as Noviol glass or Wratten 2-A filter. Behind this, on a rotor, may be mounted one or

more filters of transmission suitable for special observations, such as color analysis by filter radiometry. The ophthalmoscope is used exactly like its conventional counterpart. A source of filtered ultraviolet light (of "long wavelength," i. e., 3,650 angstrom units) is placed behind the plane of the subject's face; and the beam is directed toward the reflecting mirror, which is held in the line of vision of the subject and directed into the eye. There appears to be a number of interesting possibilities for use of the ultraviolet ophthalmoscope in medical and biologic science, not only for study of the internal ocular structures but for examination of such exposed regions as the brightly fluorescent sclera.

W. ZENTMAYER.

Neurology

BITEMPORAL HEMIANOPIA. W. O. LODGE, Brit. J. Ophth. **30:** 276 (May) 1946.

Lodge reports 3 cases of bitemporal hemianopsia. The first case was that of a girl aged 15 years with bilateral papilledema and Fröhlich's syndrome. Only the inferior nasal quadrants of the fields of vision were intact. A diagnosis of adamantinoma was confirmed histologically. The tumor was removed by a transfrontal operation. The patient died of a recurrence of the growth. The second case was that of a man aged 35. The left field of vision showed a complete temporal defect. The right field showed a central scotoma without peripheral hemianopsia; the optic disks were pale. The tumor proved to be a meningioma of the olivary eminence of the sphenoid bone. It was successfully removed, but the patient died one year later of a recurrence. The third case was one of chromophobic adenoma in a woman aged 28. The fields showed bitemporal hemianopsia. A paranasal operation was performed and a radon seed inserted. Five years later papilledema was present, and bitemporal hemianopsia recurred. The tumor was removed. One year later there was little vision in the right eye, but on the left side vision was normal. The author's approach to intrasellar tumors is a modification of the Chiari operation. The article is illustrated.

W. ZENTMAYER.

Ocular Muscles

AMBLYOPIA EX ANOPSIA IN THE ARMED FORCES. G. E. MORGAN, Am. J. Ophth. **29:** 713 (June) 1946.

Morgan analyzed 77 cases of amblyopia in the armed forces and found that the loss of vision was associated with strabismus in 56 per cent and with marked anisometropia in 30 per cent; in the remaining 14 per cent no associated etiologic factor was noted. Almost one-half the patients were seen by an ophthalmologist before the age of 7 years.

W. S. REESE.

THE TREATMENT OF CONVERGENCE DEFICIENCY, 1933-1944. S. MAYOU, Brit. J. Ophth. **30:** 354 (June) 1946.

The purpose of this somewhat lengthy article is to outline the progress made in the treatment of convergence deficiency at the Central London Ophthalmic Hospital during the past eleven years and to set

out, in somewhat greater detail, the methods developed by the author which are now employed to treat it. The subject is discussed under the headings of development of treatment, comparative methods of treatment, symptoms and causes, the psychologic approach to treatment, detailed treatment and conclusions. Under the last heading, the author states that the number of patients of all ages with convergence deficiency is large and that the symptoms, which may include migraine, are extremely unpleasant; the psychologic element is often present, and particular attention must be paid to the patient's mental approach both before and during treatment, since the successful remedy lies largely in his own hands. Care should be taken when testing and treating a patient with an esophoria, since many of these persons have a convergence deficiency as well. Even patients who are orthophoric and can actually converge may benefit from treatment, while many patients with small refractive errors are able to dispense with their correction after they have been treated. Above all, treatment can be quick and effective—on an average, two tests and five half-hour lessons—but must be taken under trained supervision; it should aim at building up voluntary convergence and teaching the patient to relax once convergence is established, since voluntary convergence alone can prevent a recurrence of the symptoms in after years. If a patient is discharged as cured after undergoing the treatment described in this article, it may be said with some certainty that, with the exception of the patient with symptoms of migraine, who may need a subsequent refresher course, the risk of his having to return for further treatment is infinitesimal.

W. ZENTMAYER.

Parasites

OCULAR MYIASIS. R. E. GIQUEAUK and R. GARCIA OCHOA, An. argent. de oftal. **5:** 79 (July-Sept.) 1944.

A discussion of myiasis in general is given. The subject of ocular myiasis is then treated, and the case of a baby 3 months old is reported. The baby was otherwise normal except for some tumefaction around the right ear. The right eye showed congestion, more intense at the caruncle and the semilunar fold. The mother had noticed that a worm came out at the inner angle and sank again into the tissues. The author could not see the worm, but by bringing a piece of cotton wet in chloroform to the inner canthus he could verify the presence of typical larvae embedded in the tissues. Worms were also found in the right ear by an otologist. All the larvae were removed by applying a cotton pledget wet in chloroform to the eye, and the child recovered uneventfully except that the conjunctivitis produced by the application of chloroform lasted for some time.

H. F. CARRASQUILLO.

Pharmacology

DETERGENTS OR WETTING AGENTS. R. J. ROTH, Am. J. Ophth. **29: 717** (June) 1946.

Roth reviews the physical and chemical characteristics of wetting agents and cites two properties that could be utilized by ophthalmologists, namely, (1) increased solubility of the drug in a solution of the proper

detergent, permitting a higher concentration of the drug in solution to come in contact with the eye, and (2) increased corneal permeability.

W. S. Reese.

Refraction and Accommodation

Report from the Wilmer Institute on the Results Obtained in the Treatment of Myopia by Visual Training. A. C. Woods, Am. J. Ophth. 29: 28 (Jan.) 1946.

Woods concludes from this interesting study of 103 persons with myopia that, with the possible exceptions of educating some patients to interpret blurred retinal images more carefully and of convincing some others that they could see better even though there was no actual improvement, the visual training given these patients was of no value for the treatment of myopia.

W. S. Reese.

Retina and Optic Nerve

Malaria Therapy in Syphilitic Primary Optic Atrophy. W. L. Bruetsch, J. A. M. A. 130: 14 (Jan. 5) 1946.

From the microscopic study of the visual pathways in 70 cases representing all types of syphilis of the central nervous system, it became apparent that primary syphilitic atrophy of the optic nerve is due to a chronic inflammatory process followed by degeneration of the nerve fibers. One of the most important effects of malarial therapy consists in arresting the inflammatory phase of the neurosyphilitic process.

Malarial therapy, besides changing the tissue immunity, inhibits the inflammatory elements of syphilitic optic nerve atrophy, and the secondary degeneration of the nerve fibers ceases. In favorable cases one course of malaria treatments will suffice. If visual failure continues to progress, one should contemplate another course of malarial therapy. Quartan malaria (Plasmodium malariae) will have to be used, since in the interim immunity has developed to the tertian strain, with which the patient was previously inoculated.

To follow up malarial therapy with injections of penicillin or to give the drug concomitantly may be worth while. To rely on penicillin alone is hazardous. Routine antisyphilitic treatment is entirely inefficacious for syphilitic optic nerve atrophy, and the patient will become blind almost as rapidly as though he had received no treatment at all.

W. Zentmayer.

Retinal Hemorrhages in Aplastic Anemia. R. J. Buxton, Brit. J. Ophth. 29: 632 (Dec.) 1945.

The patient, a Basuto aged 28, was receiving treatment for syphilis. The blood picture was that of aplastic anemia. There was no regeneration of blood cells. The optic disks showed blurring of the upper nasal edges only. The retinal vessels were normal in size and contour, with slight haziness of outline near the disk; the retina was pallid, and there was some edema about the disk. Three types of retinal hemorrhages were noted: (1) moderate-sized, flame-shaped plaques, up to 2 disk diameters in length, some with a yellowish center, which at times

glistened slightly; (2) narrow streaks about 1 disk diameter long, close to the blood vessels and (3) two or three petechial hemorrhages and one small area of exudate in the macular region.

The article is illustrated.

W. ZENTMAYER.

OCULAR SIGNS IN THE PRISONER OF WAR RETURNED FROM THE FAR EAST. G. C. DANSEY-BROWNING and W. M. RICH, Brit. M. J. 1: 20 (Jan. 5) 1946.

Of the 30 men who were released at the recapture of Rangoon, who had been prisoners of war from two to three years, 27 had beriberi. These men were examined for their ocular symptoms. Ten had bilateral central scotoma. The periphery of the field was not contracted; vision could not be brought up beyond 6/60. Examination of the fundus revealed pallor of the disks, which included primary atrophy of the optic nerve in 4 men, pallor of the papillomacular bundle in 4 and pallor of the temporal half of the disk in the remaining 8. Not 1 of these 30 men examined showed ocular symptoms of ariboflavinosis, while during the same period 2 men from the German prison camps who had not had beriberi had a definite increase in limbal vascularization.

The scotoma extended from the point of fixation to the enlarged blindspot and presented a tail. The authors cite the modern theory of the causation of tobacco-alcohol amblyopia, namely, that the condition is due to a deficiency of thiamine; at the same time, they agree to the fact that the exact nature of the deficiency of nutritional neuritis remains obscure. They think that there is a relationship between the scotoma in these cases of beriberi and the scotoma of the toxic amblyopias. As the optic nerve is a part of the central nervous system, the damage done to the nerve proper by the axial optic neuritis of beriberi is final, and any improvement of vision can be but slight.

ARNOLD KNAPP.

THROMBOSIS OF THE CENTRAL VEIN DUE TO TRAUMA: REPORT OF A CASE. R. BRÜCKNER, Ophthalmologica 109: 203, 1945.

A man aged 40 sustained two contusions of the right eye within a week. Two months later partial obstruction of the central vein occurred in this eye. The patient had been in excellent health, and no cause could be found to account for the lesion. The author assumes that the venous obstruction was due to trauma.

F. H. ADLER.

PRINCIPLES IN SURGICAL TREATMENT OF RETINAL DETACHMENTS. M. ROSENBLUM, Vestnik oftal. 25: 10, 1945.

About 1,000 operations for retinal detachment have been performed since 1933 at the von Helmholtz Institute. The Gonin and Lindner methods, which were first used, gradually gave way to diathermy. Successful results were obtained in 54.3 per cent. The patients were followed for several years. The advantages and disadvantages of various methods and operations for detachment of retina are discussed.

O. SITCHEVSKA.

Trachoma

INCIPIENT PANNUS AS A SIGN OF THE PRIMARY CORNEAL INFECTION OF TRACHOMA AND AS AN IMPORTANT CRITERION FOR THE EARLY DIAGNOSIS OF THE DISEASE. P. K. KUO, Am. J. Ophth. **29:** 645 (June) 1946.

Kuo discusses the difficulties in diagnosis of trachoma and states that careful examination with a loupe and focal illumination usually reveals neovascular sproutings from the pericorneal vascular loops of the upper overhanging limbus into the transparent part of the cornea.

W. S. REESE.

Tumors

TRANSCRANIAL REMOVAL OF INTRAORBITAL TUMORS. J. G. LOVE and W. L. BENEDICT, J. A. M. A. **129:** 777 (Nov. 17) 1945.

In a consecutive series of 35 cases of intraorbital tumor, the transcranial approach through the roof of the orbit afforded excellent visualization of the pathologic growth and the important structures within the orbit and permitted removal of tumors which it would not otherwise have been possible to remove. There was only 1 death in the series, and the results generally were good.

The Krönlein operation is useful in removal of tumors of the optic nerve without enucleation of the eyeball or in removal of encapsulated tumors situated near the apex of the orbit. For removal of tumors in this region a transcranial approach is usually to be preferred. The choice of approach must, however, at times be determined by a factor other than that of accessibility. If further decompression of the orbit is desired, it is hardly possible to get the required resection of bone with Krönlein's method, whereas by the transcranial approach not only can the entire roof of the orbit and the optic canal be removed but the lateral wall can also be resected as far as necessary.

For removal of tumors that are definitely confined to the orbit, even in the posterior third, the frontal, or the Krönlein, operation may be adequate, as has been proved many times. However, one seldom can be certain that a tumor known to be in the apical portion of the orbit does not extend beyond the orbital walls, or where its origin may be.

This paper further emphasizes the comment made by Adson and Benedict in their report of a case in which a hemangioendothelioma of the orbit was removed through a transcranial approach (ARCH. OPHTH. **12:** 484 [Oct.] 1934): "The ease with which the hemangioendothelioma was removed suggests many possibilities for the transcranial approach to vascular and neoplastic lesions situated in the retrobulbar space of the orbit."

The article is illustrated. W. ZENTMAYER.

TUMORS OF THE REGION OF THE LACRIMAL SAC. P. DESVIGNES and G. OFFRET, Arch.d'opht. **5:** 25, 1945.

Malignant tumors in the region of the lacrimal sac are rare. The authors describe 2 cases of epithelioma, in 1 of which operation had previously been performed and a small piece of the sac left. The second was a more recent case, in which histologic study revealed an epithelioma.

The diagnosis of this tumor is difficult, that in the second case being made only on operation for dacryostenosis. These 2 cases occurred within a very short time, and a little later a third case was seen, which in view of the other cases was especially interesting. The growth in this case, however, proved to be a granuloma due to a chronic inflammatory process. The result of the study of these cases emphasized the importance of completely removing the lacrimal sac at operation, leaving nothing in place and destroying as fully as possible the mucous membrane in the lacrimal canal. They also emphasize the importance of histologic examination of the tissue removed.

S. B. MARLOW.

PLEXIFORM NEUROMA OF THE LACRIMAL CARUNCLE AND CILIARY BORDER. M. BIRCH BARRAQUER, Arch. Soc. oftal. hispano-am. **4:** 245 (April) 1945.

A unique case of this condition is reported. A man aged 51 had noticed ten years before a small tumefaction in each caruncle. At the time of examination a smooth, round, pink tissue formation, about the size of a small pea, was present at the site of each caruncle, preventing the proper approximation of the lids and producing considerable epiphora. Besides, another small, regular growth was observed at the ciliary margin of each lower lid about 4 mm. from the outer canthus. These tumors were excised and examined microscopically. They showed the characteristic histopathologic picture of plexiform neuromas. The author states that this report is the only record in the literature of a similar tumor in this location. Numerous photographs and photomicrographs are shown in the article.

H. F. CARRASQUILLO.

LOCALIZATION OF INTRACRANIAL AND ORBITAL DERMOIDS. H. KRAYENBÜHL and A. E. SCHMID, Ophthalmologica **106:** 25 (May-June) 1943.

A woman aged 23 had progressively increasing unilateral exophthalmos, due to a dermoid, of hourglass shape, which extended into the middle fossa of the skull and the zygomatic temporal fossa. The differential diagnosis of orbital dermoids is discussed, and the surgical method of approach is described.

F. H. ADLER.

Uvea

TRAUMATIC ARCIFORM CHOROIDITIS. HUDELO, GUILLAUMAT and MAUSSION, Arch. d'opht. **5:** 44, 1945.

The authors present 4 observations on this condition, in 2 of which the so-called rupture of the choroid was not evident for a time after the injury. The clinical picture and the mechanism by which the process occurs are discussed. The authors propose the hypothesis that the lesion is not really a tear but, rather, represents traumatic necrosis of the choroid, perhaps trophic in nature. The arguments which support their hypothesis are the absence of the rupture in the beginning, the total absence of edema and the absence of hemorrhage.

S. B. MARLOW.

PRIMARY ATROPHY OF THE IRIS: REPORT OF A CASE. H. ARRUGA, Arch. Soc. oftal. hispano-am. **4**: 233 (April) 1945.

Arruga reports a case of this rare condition in a woman aged 25. Besides the normal pupillary opening in the right eye, which was displaced up and to the right, there were three other openings in the iris, extending from the periphery to near the margin of the pupil. The fundus could be seen through these holes. The condition had begun two years before and had gradually extended. The eye was otherwise normal. This is the only case observed by the author, and he notes that he could find only 3 cases in the literature, reported by Zentmayer, de Schweinitz and Arnold. The article is illustrated.

H. F. CARRASQUILLO.

Vision

A VISUAL TEST FOR INFANTS. J. N. EVANS, Am. J. Ophth. **29**: 73 (Jan.) 1946.

Evans suggests the use of a series of sizes of iron filings moved by a magnet under the tray to determine an infant's vision.

W. S. REESE.

DIMINUTION OF VISION IN RETURNED PRISONERS OF WAR (CORRESPONDENCE). D. FITZGERALD MOORE, Brit. M. J. **2**: 400 (Sept. 22) 1945.

Many of those who have been prisoners of war in Japanese hands have returned with the following symptoms: sore throat, cracked lips, dry skin, scaly scrotum, various nervous manifestations and, particularly, retrobulbar neuritis, which if left untreated went on to partial atrophy of the optic nerve of varying severity. From the author's experience in West Africa, where he observed this condition in the years from 1930 to 1938, particularly with regard to impaired vision, he has come to the following conclusions:

It was worth while to treat all patients having a history up to twelve months. Over that period, improvement was problematic unless the symptoms of malnutrition were still present. When the diminution of vision had not existed longer than a year, the prognosis was good, while for those who had had it six months or less it was excellent. Even in the patients who were cured asthenopic symptoms were apt to persist, and the most important symptom was photophobia. The author treated these patients with 1 ounce (31 Gm.) a day of Marmite (extract of yeast containing the vitamin B complex) for at least six months. The condition of the eye began to show improvement after a period of three to six weeks, while in some cases in which the irreversible stage had been reached no improvement occurred, though persistence in treatment was always justified. In Nigeria these symptoms were prevalent during the old government boarding school days. None of these patients became blind, but the condition remained practically stationary, in contradistinction to the progressive changes occurring with primary atrophy of the optic nerve. Absolute blindness does not occur though the vision may be very much reduced, even to perception of hand movements only.

The lesions of the mouth and skin cleared up rapidly. There is no question that a riboflavin deficiency played a major part, though probably other factors of the vitamin B complex were involved. Hence it would be wise in the general treatment to include the whole of the vitamin B complex. Brewer's yeast was not liked, while Marmite seems to have been exceedingly well taken by Africans. It is essential to regard a higher nutritional diet for these patients as an integral part of the treatment. It was quite natural that these symptoms would also become manifest under the conditions in which prisoners of war have lived in Japan. The dietary was very similar to the one in West Africa, namely, rice, manioc, occasionally sweet potatoes, a little fish, some green food and red palm oil.

ARNOLD KNAPP.

Sympathetic Ophthalmia

EARLY DIAGNOSIS OF SYMPATHETIC OPHTHALMIA. X. BULACH, Vestnik oftal. **23**: 7, 1944.

In an attempt to find early diagnostic signs of sympathetic ophthalmia, Bulach examined the blood of all patients with perforating injuries of the eye. He examined 335 patients with such injuries during 1943; 120 eyes were enucleated. Of these eyes, the process in 3 was diagnosed as sympathetic ophthalmia on pathologic examination.

An increased monocyte count was found as a rule in cases of serious bilateral iridocyclitis, panophthalmitis and endophthalmitis. There was a normal monocyte count in cases of low grade uveitis, as well as in the 3 cases of verified sympathetic iridocyclitis. Bulach, therefore, does not consider monocytosis to be of value in the diagnosis of sympathetic ophthalmia.

O. SITCHEVSKA.

Therapeutics

SUB-CONJUNCTIVAL PENICILLIN AND INTRA-OCULAR INFECTION. B. W. RYCROFT, Brit. J. Ophth. **29**: 501 (Oct.) 1945.

From a survey of the experimental evidence in the literature, Rycroft believes that certain conclusions can be reached so far as rabbits are concerned.

Direct intravitreous injections of penicillin constitute the most effective means of obtaining high concentrations and bacteriostasis in the vitreous. A single injection of purified penicillin does little harm and will control susceptible infection if given within twelve hours and will maintain bacteriostasis up to at least twenty-four hours. Multiple injections cause serious intraocular damage. Local application of drops or ointment will not result in the penetration of penicillin into the aqueous in normal eyes but will do so when the cornea is inflamed or traumatized. Iontophoresis, constant corneal baths and subconjunctival injections will maintain bacteriostatic levels in the aqueous, especially in the presence of inflammation. Intramuscular and intravitreous injections of penicillin do not produce bacteriostatic levels in the aqueous or vitreous and will not control experimental susceptible inflammation there.

It was decided to determine the value of subconjunctival injections in the treatment of intraocular infection in man. The eyes selected

either were hopelessly blind and due for removal or required conservative operation. After subconjunctival injections of 4,000 Oxford units of penicillin, the drug penetrated to the aqueous humor in 7 of the 8 cases after an interval of fifteen minutes. Failure to reach the aqueous in the one case was probably due to the short interval of aspiration after injection. Assay of the vitreous was carried out in 6 cases in 3 of which bacteriostasis appeared in forty-five minutes. The other 2 or 3 eyes were examined thirty minutes or less after injection, and this may account for the lack of inhibition. All amounts of penicillin detected in the aqueous or vitreous were above the bacteriostatic level.

Rycroft reaches the following conclusions:

Subconjunctival injection of sodium penicillin equivalent to 4,000 Oxford units will produce bacteriostasis of susceptible organisms in the aqueous humor of the human eye within one-half hour of injection. It is probable that the same state of affairs is later attained in the vitreous humor and is likely to remain for at least twenty-four hours.

Subconjunctival injections of penicillin represent a practical method by which penicillin may reach the interior of the eye. They have been widely employed without harmful effects, and the earlier they are employed the better the results.

Large doses should be employed not only because of the slow rate of diffusion but to avoid the risk of producing resistance to penicillin.

Florey has written, "Penicillin must be kept continuously in contact with all infected tissues until the natural body defenses have had time to deal with the infection." It is therefore probable that the best results of penicillin therapy for deep intraocular infection will be obtained by a combination of routes, and of these the subconjunctival is practicable and harmless. Experimental evidence stresses the importance of bringing the drug in contact with the invading organism at the earliest possible stage.

W. ZENTMAYER.

PENICILLIN IN OPHTHALMOLOGY: AN INTERIM REVIEW. A. SORSBY, Brit. J. Ophth. **29**: 511 (Oct.) 1945.

After a survey of the experimental and clinical data concerning the use of penicillin in ophthalmology, Sorsby relates his personal clinical experience. In his discussion he states that it would seem that the dosage must be determined by the causal organism rather than by the patient's tolerance. When applied in the form of drops a solution of the substance in a concentration of 2,500 units per cubic centimeter seems to be safe and in most cases adequate. For direct injection into the anterior chamber it seems for the present that 200 units in 0.25 cc. is as much as it is justifiable to give. When the drug is injected into the vitreous, it is doubtful whether it is justifiable to give more than 100 units, or even as much. Pending further clarification, subconjunctival injection seems to be the method of choice for intraocular infection, though experimental evidence does not indicate that this is a particularly satisfactory method of obtaining an adequate concentration in the interior of the eye.

W. ZENTMAYER.

PSYCHO-THERAPY IN HYSTERICAL AMBLYOPIA. P. D. GIRIDHAR, Indian J. Ophth. **6:** 32 (July) 1945.

Giridhar stresses that hysterical amblyopia is in fact a psychopathic disease in which the patient forgets that he can see and vision is said to be lost, but that when the patient is convinced that he can actually see he indeed begins to see. The disease is mental rather than physical, and the apparent loss of vision can be restored by a tactful and psychic handling of the patient.

Four cases are recorded, in all of which vision was restored by suggestion and by subconjunctival injections of saline solutions.

W. ZENTMAYER.

LOCAL USES OF PENICILLIN IN OPHTHALMOLOGY. K. KRISHNAMURTY, Indian J. Ophth. **6:** 34 (July) 1945.

In this article Krishnamurty deals with the local use of penicillin only. Penicillin in the form of an ointment has been found superior to powder or drops. The ointment should be applied six times daily. In cases of conjunctivitis clinical cure occurs within forty-eight hours. In cases of trachoma, redness, watering of the eyes, blepharospasm and photophobia disappear in the first week, and in the second week the granules begin to flatten. In the third week the process of scarring appears.

W. ZENTMAYER.

Toxic Amblyopia

SEVERE AMAUROSIS DUE TO QUININE POISONING: REPORT OF A CASE. R. ANTOINE, R. LEGROUS and P. STRICKER, Arch. d'opht. **5:** 349, 1945.

The authors describe a case of amaurosis due to quinine poisoning which came on rapidly, with marked constriction of the fields of vision. Their purpose in presenting the case is to demonstrate the beneficial action of acetylcholine. The rapid improvement occurred after four infiltrations into the superior cervical sympathetic ganglion. The fields of vision were not reestablished spontaneously but were restored to normal only on repeated treatment of the sympathetic ganglion. The first return of vision was the perception of light, and then vision was restored in the temporal field. The authors discuss the distribution of the blood supply of the optic nerve and the chiasm in relation to this condition. The intermingling of the sympathetic fibers is an important consideration in treatment with the vasodilator drugs.

S. B. MARLOW.

Book Reviews

Cirugía ocular. By H. Arruga. Pp. 888. Barcelona, Spain: Salvat Editors, S.A., 1946. Price 380 pesos.

The author, well known in Europe and the Continent for his skill as an ophthalmic surgeon, has brought together in this volume the fruits of his wide knowledge and experience. This book is essentially a practical treatise, in which Arruga gives credit to the numerous writers whose methods he describes. A number of his own ingenious instruments and surgical procedures are presented.

After a chapter dealing with the general principles of ocular surgery, Arruga, in a systematic fashion, treats of the surgery of the eyelids, lacrimal apparatus, conjunctiva, cornea, sclera, iris, ciliary body and choroid, lens, extraocular muscles, eyeball, vitreous and orbit and the operative treatment of detachment of the retina, glaucoma and intraocular foreign bodies. The chapters dealing with the lacrimal passages, cataract extraction and detachment of the retina are outstanding, in the opinion of the reviewer; but the remaining sections are valuable.

It is only to be expected that some American ophthalmologists will not agree with all of Arruga's statements. For example, the author, in his chapter on the extraocular muscles, does not favor tenotomy or myectomy of the inferior oblique muscle by way of an incision in the inferior conjunctival cul-de-sac; nor does he recommend any operative procedure on this muscle at its insertion into the globe.

The book is beautifully printed and contains 1,218 illustrations, of which 119 are in color. In the excellence and clarity of the drawings, this volume is a superb contribution to the world's ophthalmologic literature. It is to be hoped that the author will arrange for an English translation, and thus further cement the friendly bonds which link ophthalmologists in this country with their Spanish-speaking colleagues.

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